INTRA-ARTICULAR PLATELET RICH PLASMA VS HYALURONIC ACID IN TREATMENT OF OSTEOARTHRITIS OF KNEE." -A COMPARATIVE STUDY.

by

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Dissertation submitted to

B.L.D.E. (Deemed to be) UNIVERSITY VIJAYAPURA, KARNATAKA

In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY

IN

ORTHOPAEDICS

Under the guidance of

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ACKNOWLEDGEMENT

On completion of my post-graduation journey and this scientific document, I would like to acknowledge the immense help received from my mentors in the department of Orthopaedics. With privilege and respect, I would like to express my gratitude and indebtedness to my Guide, Dr. Dayanand. B. B, Professor, Department of Orthopaedics and for his constant inspiration, extensive encouragement and loving support, which rendered in pursuit of my post-graduate studies and in preparing this dissertation.

I am forever grateful to Dr. S. S. Nandi, Professor and HOD of Department of Orthopaedics, Shri B.M Patil Medical College, Hospital and Research Centre, Vijayapura for his valuable suggestions, support and encouragement throughout the post graduate programme.

I am grateful to all my teachers in the Department of Orthopaedics for their guidance, encouragement and inspiration.

I am extremely grateful to Dr. Shivanand L Karigar department of anastesiology , Shri B. M Patil Medical College, Hospital and Research Centre, Vijayapura for his valuable suggestions, support and encouragement in completing my study.

I am extremely thankful to Professor Dr. Aravind Patil, Principal, of B.L.D.E.(DU) Shri. B.M. Patil Medical College, Hospital and Research Centre, Vijayapura, for permitting me to utilize resources in completion of my work.

My thanks to one and all staff of Library, Orthopaedics Department and Hospital for their co-operation in my study I am thankful to the members of ethical committee BLDEU's Shri. B. M. Patil Medical College Hospital and Research Centre Vijayapur for permitting me to carry out this study.

I am thankful to Dr Vijaya Sorganvi for her help in statistical analysis. I also like to thank all my batchmates, seniors and juniors for their help and cooperation.

I would like to express my deep-felt gratitude to my parents for their constant support and encouragement throughout.

Last but not least, I convey my heartfelt gratitude to all my patients; withoutwhose co-operation, this study would be incomplete.

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Intraarticular PRP vs Hyaluronic acid in treatment of osteoarthritis of knee -A comparative

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Document Details

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trn:oid:::3618:87488307

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ABSTRACT

Introduction: Osteoarthritis (OA) of the knee is a prevalent degenerative joint disease characterized by progressive cartilage deterioration, pain, and functional limitation. Intra-articular injections of biologic agents have emerged as potential disease-modifying interventions for knee OA. This study aimed to compare the efficacy and safety of intra-articular platelet-rich plasma (PRP) versus hyaluronic acid (HA) in the treatment of mild to moderate knee OA.

Methods: In this prospective comparative study, 70 patients with Kellgren-Lawrence grade 1-2 knee OA were randomly allocated to receive either PRP (n=35) or HA (n=35) intra-articular injections. Patients were evaluated at baseline, 3 months, and 6 months post-injection using the Visual Analog Scale (VAS) for pain and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for functional assessment. Complications and adverse events were recorded throughout the follow-up period.

Results: Demographic characteristics were comparable between groups. At 3 months, the HA group showed significantly better pain reduction (VAS: 3.12±0.48 vs 4.65±0.68; $p<0.001$) and functional improvement (WOMAC: 31.7±4.3 vs 47.2±5.4; $p<0.001$) compared to the PRP group. However, at 6 months, the pattern reversed, with the PRP group demonstrating superior pain relief (VAS: 2.08±0.45 vs 3.14±0.51; $p<0.001$) and functional outcomes (WOMAC: 22.11±3.2 vs 32.4±4.6; $p<0.001$). The PRP group exhibited a better safety profile with no cases of infection or synovitis, compared to the HA group which reported infection (5.7%) and synovitis (11.4%).

Conclusion: Intra-articular PRP and HA demonstrate a distinct temporal efficacy pattern in knee OA management, with HA providing superior short-term benefits at 3 months and PRP showing significantly better long-term outcomes at 6 months. PRP also exhibited a more favorable safety profile. These findings suggest that PRP may be the preferred option for long-term management of mild to moderate knee OA, particularly in patients seeking sustained symptom relief and functional improvement.

Keywords: Osteoarthritis; Knee; Platelet-rich plasma; Hyaluronic acid; Intra-articular injection; Visual Analog Scale; WOMAC; Regenerative medicine; Viscosupplementation; Biologic therapy

ABBREVIATIONS

BMI - Body Mass Index

ECM - Extracellular Matrix

FGF - Fibroblast Growth Factor

HA - Hyaluronic Acid

IGF-1 - Insulin-like Growth Factor-1

IL - Interleukin

KL - Kellgren-Lawrence

MMPs - Matrix Metalloproteinases

NSAIDs - Non-Steroidal Anti-Inflammatory Drugs

OA - Osteoarthritis

PDGF - Platelet-Derived Growth Factor

PRP - Platelet-Rich Plasma

RANTES - Regulated upon Activation, Normal T Cell Expressed and Presumably Secreted

SD - Standard Deviation

TGF-β - Transforming Growth Factor-beta

TNF-α - Tumor Necrosis Factor-alpha

VAS - Visual Analog Scale

VEGF - Vascular Endothelial Growth Factor

WOMAC - Western Ontario and McMaster Universities Osteoarthritis Index

INTRODUCTION

Osteoarthritis (OA) of the knee is one of the most prevalent chronic degenerative joint disorders, affecting millions globally and significantly impacting quality of life.[1] As the world's population ages, the burden of knee OA continues to grow, with current estimates suggesting that approximately 10-15% of adults over the age of 60 experience symptomatic knee OA.[2] The condition is characterized by progressive deterioration of articular cartilage, subchondral bone remodeling, and chronic inflammation, leading to pain, stiffness, and reduced joint function.

The management of knee OA has traditionally followed a stepwise approach, beginning with conservative measures such as lifestyle modifications, physical therapy, and oral medications. However, these conventional treatments often provide only temporary relief and may be associated with significant side effects, particularly with long-term use.[3] This has led to an increasing interest in minimally invasive, potentially disease-modifying treatments that could offer better outcomes for patients with knee OA.

Among the emerging therapeutic options, intra-articular injections have gained considerable attention in recent years. Two particularly promising treatments are Platelet-Rich Plasma (PRP) and Hyaluronic Acid (HA). PRP, derived from the patient's own blood, contains a concentrated mixture of growth factors and bioactive proteins that are believed to promote tissue healing and regeneration.[4] The theoretical basis for PRP use in OA stems from its potential to modulate inflammation, stimulate cell proliferation, and enhance extracellular matrix synthesis in cartilage tissue.[5]

Hyaluronic Acid, on the other hand, is a naturally occurring glycosaminoglycan that plays a crucial role in maintaining the viscoelastic properties of synovial fluid. Its therapeutic use in knee OA is based on its ability to improve joint lubrication, reduce inflammation, and potentially provide chondroprotective effects.[6] Several studies have demonstrated the efficacy of HA injections in reducing pain and improving function in patients with knee OA, although the

duration of these benefits remains a subject of ongoing research.[7]

The growing body of evidence supporting both PRP and HA has led to their increased adoption in clinical practice. However, there remains considerable debate regarding their relative efficacy, optimal timing of administration, and cost-effectiveness. While some studies suggest that PRP may offer superior long-term outcomes compared to HA[8], others have found comparable results between the two treatments. The variability in PRP preparation protocols, injection techniques, and patient selection criteria has made it challenging to draw definitive conclusions about their comparative effectiveness.

Furthermore, the biological mechanisms underlying the therapeutic effects of both PRP and HA are not fully understood. PRP's complex composition, containing various growth factors such as PDGF, TGF-β, and VEGF, makes it difficult to determine which components are primarily responsible for its clinical benefits.[9] Similarly, while HA's mechanical properties are well-documented, its biological effects on cartilage metabolism and inflammation require further investigation.

The economic implications of these treatments also warrant consideration. While PRP preparation requires specialized equipment and processing of autologous blood, HA products are commercially manufactured and readily available. However, the need for multiple HA injections compared to potentially fewer PRP sessions may influence the overall cost-effectiveness of these treatments.[10]

Given the significant impact of knee OA on public health and the continuing evolution of treatment options, there is a critical need for well-designed comparative studies to guide clinical decision-making. This research aims to contribute to the existing knowledge base by conducting a comprehensive comparison of PRP and HA in the treatment of knee OA, focusing on clinical outcomes, safety profiles, and patient satisfaction.

AIM & OBJECTIVES

Objectives:

1. To research the use of platelet-rich plasma and intra-articular hyaluronic acid in the treatment of osteoarthritis in the knee.
2. To assess PRP's effectiveness and safety in treating mild to moderately symptomatic knee osteoarthritis compared to hyaluronic acid.
3. Research side effects of intra-articular injections used to treat osteoarthritis.

REVIEW OF LITERATURE

OSTEOARTHRITIS OF KNEE JOINT

Weight-bearing joints like the knees are especially affected by osteoarthritis (OA), a chronic degenerative joint condition marked by osteophyte (abnormal bony growth) development and cartilage degradation.[11]

Brief Historical Aspects[12]

What's in a name? The fight for OA's clinical and pathological independence

When Heberden separated "digitorum nodi" from gout and rheumatoid arthritis (RA) in 1816, the history of osteoarthritis (OA) terminology began. The word "osteo-arthritis" was first used by Archibald Garrod in 1890, but it is generally accepted that he preferred the term "arthritis deformans." Richard von Volkmann first used the name "OA" in the middle of the 1850s, when he made a clear anatomical and clinical distinction between OA and RA. However, Charcot and Trastour's 1853 theory—which Virchow endorsed—that OA and RA were distinct degrees of the same illness eclipsed his findings. “The word OA may have been introduced in 1863 by the Nomenclature Committee of the Royal College of Physicians of London.” The distinction between RA's secondary synovial problems and OA's main bone/cartilage abnormalities was not commonly accepted until the middle of the 20th century. The preferred name was "arthritis deformans" until that point.

The changing faces of OA: from ‘wear-and-tear’ to inflammatory remodelling

The persistent, proliferative, noninfectious inflammation known as osteo-arthritis deformans causes the joint to gradually deteriorate. The primary cause of the inflammation is the joint's changed and compromised function. The joint may be directly or indirectly affected by mechanical stress.

Although contemporary literature frequently implies that OA was formerly thought to be just "wear-and-tear" and that the whole-joint notion was new, historical data reveals a more complex perspective. Most doctors agreed with Garrod's 1924 comprehensive picture of OA impacting many joint components throughout time, even though surgeon William Arbuthnot (1846-1943) saw OA as a straightforward age-dependent cartilage disintegration. OA was eventually recognised as a systemic disorder after the "wear-and-tear" idea was resurrected to contrast with the contemporary understanding of the disease as whole-joint failure, comparable to organ failure.

Beyond the joint: OA as a neurogenic-immune homeostatic disorder

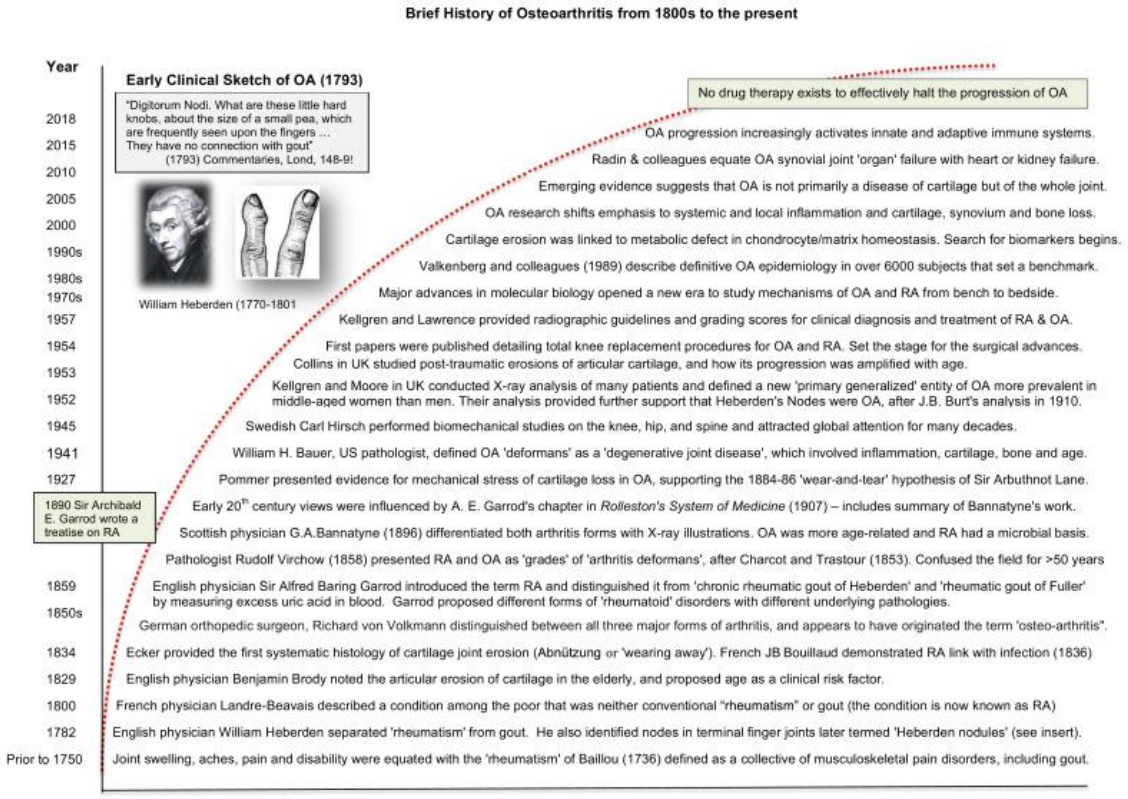
Interestingly, doctors suggested a link between arthritis and the central nervous system (CNS) in the late 1880s, citing findings of higher resting heart rates that suggested vagal nerve dysfunction. Four main symptoms were listed in John Spender's 1889 book: skin discolouration, vasomotor problems, accelerated cardiac action with potential vagus nerve involvement, and particular brain symptoms. When defining OA patients nowadays, many of these clinical characteristics are still applicable.

The involvement of the CNS in OA was not fully understood throughout the 20th century. The 1950s saw significant advancements in electrophysiology, pharmacology, and neural tracing, which resulted in the discovery of the Nucleus Tractus Solitarius (NTS) and the hypothalamic-pituitary-adrenal axis. Through sympathetic-parasympathetic balance, the NTS controls a number of body processes, such as blood flow, metabolism, inflammation, and heart rate.

Subtle alterations in sympathetic tone have been found to be important in the course of OA in

recent studies. By changing the local neurotransmitter microenvironment, modifications in sympathetic nerve firing patterns may lessen pain and decrease the progression of disease. The strong innervation of bone and joint tissues by sympathetic and sensory nerves, which can control vascularization, inflammation, and bone mass, lends credence to this notion. According to recent research, osteoblasts may serve as environmental sensors that connect to the central nervous system through afferent neurones.

This neurological association is supported by clinical data, which indicates that alpha and beta-adrenergic blockers may lessen pain and structural alterations in knee OA patients over a 24-month period when compared to non-users. By modifying the synaptic 'tune' of injured joints and their feedback pathways to the central system, our findings imply that combining cutting-edge bioelectronic technology with neuropharmacological drugs may help delay the progression of OA.
Figure 1: An overview of the development of osteoarthritis (OA) that demonstrates its increasing pathological and clinical independence from gout and rheumatoid arthritis (RA). A wealth of information on the development of new techniques and knowledge can be found in history, which also shows how vibrant and perceptive many of the early scholarly debates on arthritis were in comparison to the current. We still don't fully understand the underlying aetiology of OA and haven't found a solution, despite remarkable advancements over the previous 200 years.

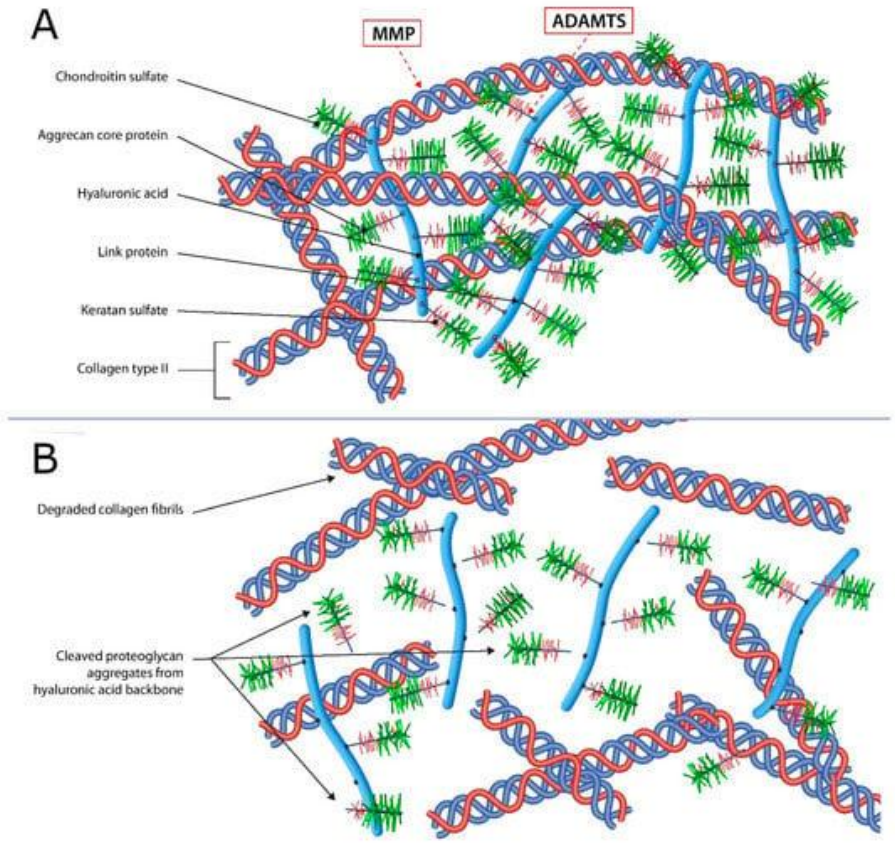


Articular Cartilage[13]

Chondrocytes are the sole cell type found in articular cartilage (AC), which is an avascular, alymphatic, and aneural tissue. "The extracellular matrix (ECM), which is made up of water (more than 70%) and organic materials like type II collagen, aggrecan, other proteoglycans (decorin, biglycan, and fibromodulin), collagens (types III, VI, IX, XI, etc.), glycosaminoglycans, and glycoproteins, helps to form AC in addition to chondrocytes." "Entrapped in a network of cross-linked type II collagen fibrils are proteoglycan aggregates, which are composed of negatively charged glycosaminoglycans (keratan sulphate and chondroitin sulphate) attached to the aggrecan core protein, which is connected to the hyaluronic acid backbone, along with other matrix constituents" Cartilage development is impacted by the premature termination codon on aggrecan mRNA, and type II collagen may be indirectly impacted by an inability to produce aggrecan, indicating a potential feedback regulation between the extracellular matrix and type II collagen. "There is a noticeable change in the matrix structure surrounding chondrocytes, where additional proteins including collagen VI, fibromodulin, and matrilin 3 form the pericellular matrix, despite

the fact that type II collagen and aggrecan are the most prevalent proteins in the cartilage matrix." Chondrocytes produce all of the components of cartilage, and they are essential for preserving the cartilaginous environment because they balance the synthesis of ECM components and the enzymes that break them down, resulting in a limited and balanced turnover between anabolic and catabolic activities. Mechanoreceptors on the cell surface sense mechanical loading, which stimulates AC metabolism. The metabolic activity of chondrocytes is modulated by mechanical signals through the process of mechanotransduction, which triggers the creation of chemicals to maintain tissue integrity. Integrins and mechanosensitive ion channels are examples of surface mechanoreceptors. Transmembrane proteins called integrins bind chemical substances like growth factors and cytokines to initiate internal cell signalling. The process of tissue remodelling is brought on by the activation of these mechanoreceptors, which starts intracellular signalling cascades. Additionally, the biomechanical stimulation produced by dynamic compression during moderate exercise can control the metabolic balance, inhibit the advancement of cartilage deterioration, and decrease the manufacture of proteolytic enzymes. "The fact that inadequate biomechanical stimuli, like immobilisation, can result in decreased thickness (>10%) and softness of AC in the knee joint in the absence of normal joint loading highlights the significance of appropriate mechanical loading." The most obvious triggering cause of OA, on the other hand, is excessive mechanical loading, which causes a quantitative imbalance between anabolic and catabolic activity, depletes matrix components, and causes irreversible destruction due to a lack of AC regenerative capacity.

Figure 2: The extracellular matrix of cartilage and its alterations in osteoarthritis are shown schematically. (A) Type II collagen fibres are intertwined with a robust network of proteoglycan aggregates. Red arrows indicate matrix metalloproteinases (MMPs) and a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS) cleavage sites; (B) Osteoarthritis-related changes in the cartilage matrix are indicated by the cleavage of type II collagen fibres by ADAMTS and the breakdown of proteoglycans by MMPs.



"The superficial (tangential) zone, intermediate (transitional) zone, deep (radial) zone, and a highlymineralised zone of calcified cartilage are the four layers that make up AC." A histologically defined zone known as the tidemark separates the calcified zone from the unmineralized upper cartilage layers and separates the cartilage from the subchondral bone underneath. The orientation of collagen fibrils and the shape and location of chondrocytes define the layers. Collagen fibrils are orientated horizontally and chondrocytes are disk-shaped in the superficial zone. The intermediate zone contains randomly distributed spherical chondrocytes and diagonally orientated collagen fibrils. Collagen fibrils arranged radially and vertical columns of chondrocytes define the deep zone. Collagen fibrils are positioned perpendicular to the articular surface in calcified cartilage. There are hardly many chondrocytes in this area. They have a rounded form and are not positioned precisely.

Synovium[13]

The synovium is composed of synovial fluid and the synovial membrane. An essential component of cartilage nourishment is synovial fluid. The synovial fluid serves as both a reservoir for the avascular cartilage's breakdown products and a source of nutrition. In healthy people, the intima (lining layer) and subintima (sublining layer) that make up the synovial membrane can be up to 5 mm thick. Over vascularised loose connective tissue, two to three layers of metabolically highly active cells (synoviocytes) create the subintima, which is rich in fibroblasts that secrete collagen. Classic and inflammatory-like macrophages are the two varieties of macrophages that have been identified in synovia. Since they generate VEGF, which could be a potential mechanism generating inflammation and synovitis, inflammatory macrophages are significant mediators in knee OA. In addition to being CD163- and CD68-positive, macrophage-like synoviocytes also exhibit positive staining for nonspecific esterase, an enzyme histochemical stain that distinguishes from other cell types. Together with CD55-positive fibroblast-like synoviocytes that express class II major histocompatibility molecules, they constitute an essential component of the intima. While fibroblast-like synoviocytes are located farther from the intima and mostly produce hyaluronic acid, macrophage-like synoviocytes multiply during inflammation. During exercise, the synovium maintains the volume of synovial fluid by producing hyaluronan and a plasminogen activator. Additionally, it secretes hyaluronic acid and lubricin, which are crucial components of synovial fluid.

Infrapatellar Fat Pad, Menisci, Periarticular Muscles, Ligaments and Tendons[13]

Hoffa's infrapatellar fat pad (IPFP), the biggest intraarticular adipose structure, is situated between the joint capsule and the synovium in the anterior knee compartment. Hoffa's fat pad functions as a shock absorber, lessening the force of loading and preventing mechanical harm to the knee. Adipocytes, fibroblasts, leukocytes, macrophages, and other immune cells are found in IPFP, an extremely sensitive tissue.

Epidemiology

The most frequent type of arthritis identified is osteoarthritis of the knee, and as life expectancy and obesity increase, so will its prevalence. At 14% to 18% in adults and 20% to 27% in those aged 40 and above, OA is the second most prevalent rheumatologic condition in the world. 14 According to several sources, symptomatic knee osteoarthritis affects about 10% of men and 13% of women aged 60 and beyond. The frequency increases to as much as 40% among people over 70. Males are also less likely than females to have osteoarthritis in their knees. It's interesting to note that not everyone with radiographic evidence of osteoarthritis in the knee will exhibit symptoms.[15]

Indian Scenario- According to several research conducted in India, between 20% and 40% of people have OA. Pal et al. conducted a community-based cross-sectional survey throughout India and found that 28.7% of people had knee OA, with the Kellgren and Lawrence scale being used to identify the condition. 16 Jadhao et al. diagnosed OA in rural Maharashtra, India, using the ACR criteria, and they came to the conclusion that the prevalence was 34.7%. 17 Venkatachalam et al. also determined that the prevalence of OA in rural Tamil Nadu, South India, was 27.1% based on ACR criteria. 18 OA is more frequent in women, and its prevalence rises with age. Significant mobility impairment is caused by OA, especially in women, and the illness is more common in women over 45.[19]

Etiology

"Depending on its cause, osteoarthritis in the knee can be categorised as primary or secondary. Unknown causes of articular cartilage deterioration lead to primary osteoarthritis in the knee. Usually, this is regarded as deterioration brought on by ageing and wear and tear. Degeneration of the articular cartilage for a known cause causes secondary osteoarthritis in the knee."[20, 21]

“Possible Causes of Secondary Knee OA

- Posttraumatic
- Postsurgical
- Congenital or malformation of the limb
- Malposition (varus/valgus)
- Scoliosis
- Rickets
- Hemochromatosis
- Chondrocalcinosis
- Ochronosis
- Wilson disease
- Gout
- Pseudogout
- Acromegaly
- Avascular necrosis
- Rheumatoid arthritis
- Infectious arthritis
- Psoriatic arthritis
- Hemophilia
- Paget disease
- Sickle cell disease”

“Risk Factors for Knee OA

Modifiable

- Articular trauma
- Occupation – prolonged standing and repetitive knee bending
- Muscle weakness or imbalance
- Weight
- Health – metabolic syndrome

Non-modifiable

- Gender - females more common than males
- Age
- Genetics
- Race”

Pathophysiology

The main constituents of articular cartilage are water, chondrocytes, proteoglycans, and type II collagen. “In order to ensure that any cartilage breakdown is balanced by synthesis, healthy articular cartilage continuously maintains equilibrium between all of its constituent parts. Thus, healthy articular cartilage is preserved. Degradative enzymes called matrix metalloproteases (MMPs) are overexpressed during osteoarthritis, upsetting the balance and leading to a general loss of collagen and proteoglycans. Early in the course of osteoarthritis, chondrocytes try to match the degradative process by increasing the synthesis of proteoglycans and secreting tissue inhibitors of MMPs (TIMPs). This reparative procedure is insufficient, though.” Despite increased synthesis, increased water content, the disordered pattern of collagen, and eventually the loss of articular cartilage flexibility, the imbalance leads to a decrease in the amount of proteoglycans. On a macroscopic level, these alterations cause the cartilage to crack and fracture, which eventually leads to the articular surface eroding. [22]

While there is a strong correlation between knee osteoarthritis and ageing, it is crucial to remember

that knee osteoarthritis is a disease in and of itself rather than merely a result of ageing. The variations in cartilage observed with osteoarthritis and ageing lend credence to this. Moreover, knee osteoarthritis exhibits increased expression of the enzymes that break down cartilage, while normal ageing cartilage exhibits normal levels of these enzymes.

Figure 3: Pathogenesis of Osteoarthritis

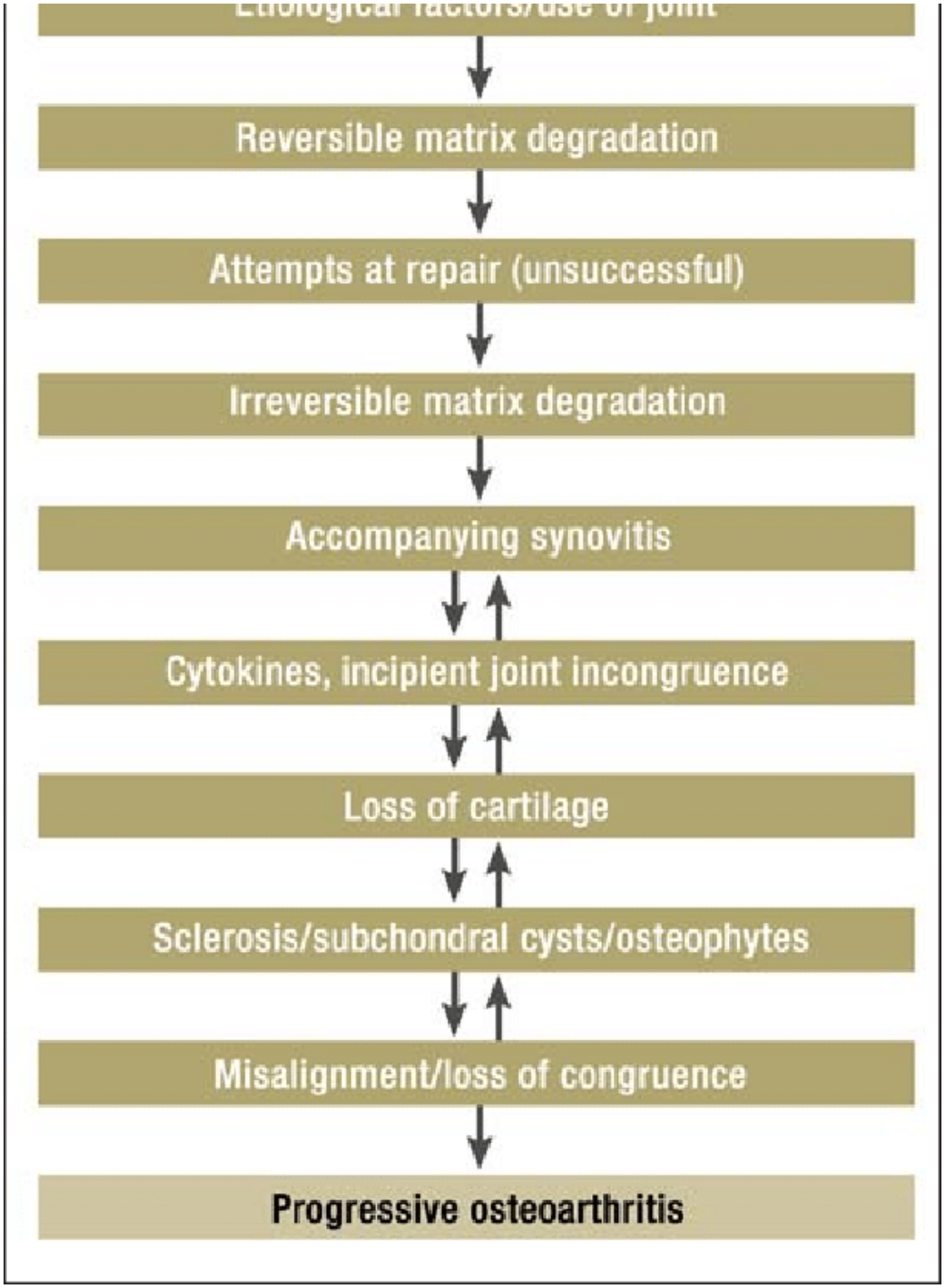
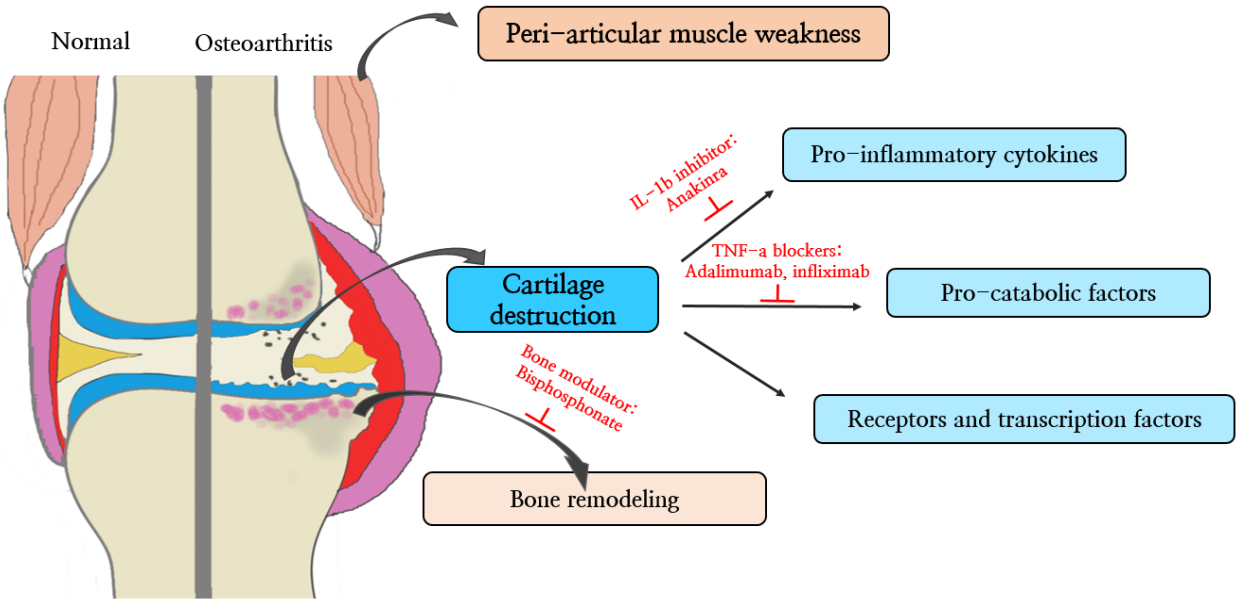


Figure 4: Pathophysiology of Osteoarthritis



"Histopathology

Cartilage Changes in Aging[23]

- Water content – decreased
- Collagen – same
- Proteoglycan content – decreased
- Proteoglycan synthesis – same
- Chondrocyte size – increased
- Chondrocyte number – decreased
- Modulus of elasticity – increased

Cartilage Changes in OA

- Water content – increased
- Collagen – disorganized
- Proteoglycan content – decreased
- Proteoglycan synthesis – increased
- Chondrocyte size – same
- Chondrocyte number – same
- Modulus of elasticity – decreased

Matrix Metalloproteases

Responsible for cartilage matrix degradation

- Stromelysin
- Plasmin
- Aggrecanase-1 (ADAMTS-4)
- Collagenase
- Gelatinase

Tissue Inhibitors of MMPs

Control MMP activity preventing excess degradation

- TIMP-1
- TIMP-2
- Alpha-2-macroglobulin"

History and Physical

Knee pain is frequently the primary complaint of patients when they visit their healthcare physician. As a result, getting a thorough history of their symptoms is crucial. Because knee pain can originate from either the hip joint or the lumbar spine, pay close attention to the history. To determine any risk factors linked to secondary knee OA, a thorough medical and surgical history is equally crucial.

"The history of the present illness should include the following:

- Onset of symptoms
- Specific location of pain
- Duration of pain and symptoms
- Characteristics of the pain
- Alleviating and aggravating factors
- Any radiation of pain
- Specific timing of symptoms

- Severity of symptoms
- The patient's functional activity

Clinical Symptoms of Knee OA

Knee Pain

- Typically of gradual onset
- Worse with prolonged activity
- Worse with repetitive bending or stairs
- Worse with inactivity
- Worsening over time
- Better with rest
- Better with ice or anti-inflammatory medication
- Knee stiffness
- Knee swelling
- Decreased ambulatory capacity”

Visual inspection should be the first step in any physical examination of the knee. When the patient is upright, check for varus or valgus deformities, quadriceps muscle atrophy, and periarticular erythema and oedema. Keep an eye on your gait for any indications of pain or unusual knee joint motion, which may point to ligamentous instability. Next, check the surrounding skin for soft tissue lesions, underlying trauma evidence, and scars from prior surgeries, as well as their placement.

Testing for range of motion (ROM) is a crucial component of the knee examination. It is important to measure and record both active and passive range of motion in relation to flexion and extension.

A vital component of any knee examination is the palpation of the soft tissue and bone structures. The knee's medial, midline, and lateral structures can all be examined palpatorily.

“Areas of Focus for the Medial Aspect of the Lnee

- Vastus medialis obliquus
- Superomedial pole patella
- Medial facet of the patella
- Origin of the medial collateral ligament (MCL)
- Midsubstance of the MCL
- Broad insertion of the MCL
- Medial joint line
- Medial meniscus
- Pes anserine tendons and bursa

Areas of Focus for the Midline of the Knee

- Quadricep tendon
- Suprapatellar pouch
- Superior pole patella
- Patellar mobility
- Prepatellar bursa
- Patellar tendon
- Tibial tubercle

Areas of Focus for the Lateral Aspect of the Knee

- Iliotibial band
- Lateral facet patella
- Lateral collateral ligament (LCL)
- Lateral joint line
- Lateral meniscus
- Gerdy’s tubercle”

A comprehensive neurovascular examination must to be carried out and recorded. It's critical to

evaluate the quadriceps and hamstrings' strength because knee discomfort frequently causes these muscles to weaken. Given the possibility of concurrent neurogenic complaints, a sensory examination of the femoral, peroneal, and tibial nerves should be performed. It is crucial to palpate the popliteal, dorsalis pedis, and posterior tibial pulses since any irregularities could indicate vascular issues.

Depending on the clinical suspicion derived from the history, further knee tests could be conducted.

"Special Knee Tests

- Patella apprehension – patellar instability
- J-sign – patellar maltracking
- Patella compression/grind – chondromalacia or patellofemoral arthritis
- Medial McMurray – a medial meniscus tear
- Lateral McMurray – lateral meniscus tear
- Thessaly test – a meniscus tear
- Lachman – anterior cruciate ligament (ACL) injury
- Anterior drawer – ACL injury
- Pivot shift – ACL injury
- Posterior drawer – posterior cruciate ligament (PCL) injury
- Posterior sag – PCL injury
- Quadriceps active test – PCL injury
- Valgus stress test – MCL injury
- Varus stress test – LCL injury"

Evaluation

Radiographic imaging is necessary in addition to a comprehensive history and physical examination. A skyline view of the patella, standing lateral in extension, and standing anteroposterior (AP) are the recommended views. The knee's weight-bearing surface can be better evaluated by obtaining a standing 45-degree posteroanterior (PA) view of the knee. In order to assess the degree of deformity and general alignment of the lower extremities, long leg standing films are occasionally acquired. It is crucial to know that the patient must be standing when obtaining knee radiographs. This provides a realistic depiction of the current joint space narrowing. Films are frequently taken while the patient is supine, which provides an inaccurate impression of joint alignment and space and shouldn't be utilised to assess suspected knee OA.[24, 25]

Radiographic Findings of OA

- Joint space narrowing
- Osteophyte formation
- Subchondral sclerosis
- Subchondral cysts

Based on its aetiology, OA is divided into two categories: primary (idiopathic or non-traumatic) and secondary (often brought on by trauma or mechanical misalignment). The 1957 Kellgren–Lawrence (KL) system can also be used to classify the disease's severity based on radiographic evidence.[26]

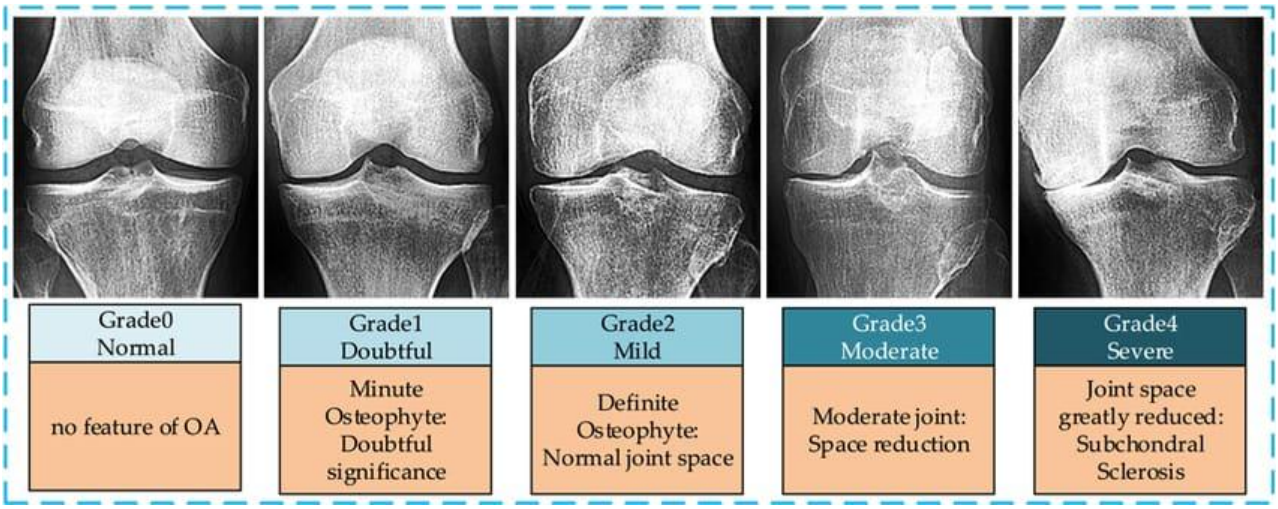


Figure 5: Kellgren–Lawrence (KL) system

Treatment

It is doubtful that OA will regress and restore damaged structures because it is a progressive and degenerative condition. Therefore, the goal of current therapeutic techniques is to control symptoms, unless the severity of the condition necessitates joint replacement surgery[27].

To standardise and suggest the available treatment alternatives, several academic and professional associations have currently developed several guidelines (Table 1). "These include papers from the American Academy of Orthopaedic Surgeons (AAOS), the American College of Rheumatology (ACR), and the Osteoarthritis Research Society International (OARSI). OARSI (Osteoarthritis Research Society International), ACR (American College of Rheumatology), AAOS (American Academy of Orthopaedic Surgeons), TENS (transcutaneous electrical nerve stimulation), and NSAIDs (non-steroidal anti-inflammatory drugs) are among the societies' recommendations for managing osteoarthritis in the knee."[28, 30])

Societies recommendations			
Treatment	**OARSI**	**ACR**	**AAOS**
Exercise (land and water based)	Appropriate	Strong recommendation	Strong recommendation
Transcutaneous electrical nerve stimulation (TENS)	Uncertain	Conditional recommendation	Inconclusive
Weight control	Appropriate	Strong recommendation	Moderate recommendation
Chondroitin or Glucosamine	Not appropriate for disease modification, Uncertain	Recommended against use	Recommended against use
Acetaminophen	Without comorbidities: appropriate	Conditional recommendation	Inconclusive
Duloxetine	Appropriate	No recommendation	No recommendation
Oral NSAIDs	Without comorbidities: appropriate With comorbidities: not appropriate	Conditional recommendation	Strong recommendation
Topical NSAIDs	Appropriate	Conditional recommendation	Strong recommendation

Opioids	Uncertain	No recommendation	Recommended only tramadol
Intra-articular corticosteroids	Appropriate	Conditional recommendation	Inconclusive
Intra-articular viscosupplementation	Uncertain	No recommendation	Recommended against use

Non-pharmacological management

Controlling the excruciating signals coming from these joints is the goal of OA treatment, but improving functionality and quality of life is even more important. The primary line of treatment for knee OA should always be non-pharmacological approaches. [31]

The health of the knee joint is negatively impacted by inactivity and disuse; the lack of mechanical stimulation causes the cartilage to soften and thin more quickly, lowers the amount of glycosaminoglycan in the cartilage, and impairs joint flexibility and mechanics. For this patient population, light-to-moderate physical activity offers several advantages, including improved mood and self-efficacy, decreased risk of diabetes, cardiovascular events, falls, and disability, in addition to mechanical and functional improvements. [32]

"To improve success, exercise regimens should be customised to each patient's requirements, tolerance, and preferences; high-impact activities should be avoided; and long-term adherence should be optimised. [33] Patients with knee OA have been found to benefit from various exercise modalities (Table 2); routines should be done three times a week, and the patient should finish at least 12 sessions to gauge response."[31]

Given the lower joint impact, aquatic (water-based) therapies offer a substitute for individuals who are reluctant to begin land-based workouts. When beginning weight-bearing activities, some patients may experience a worsening of their symptoms, whereas others may be able to handle aquatic therapy better. Once the patient no longer fears moving, some doctors use this therapy as a

transitional approach to land-based modalities..[34]

"Weight management plays an important role in symptom management, and it has been noted that the benefit of exercise is potentiated by the reduction of weight.[16] Obesity can predispose patients to suffer from knee OA, it has deleterious molecular and mechanical effects. The adipose tissue itself is a source of inflammatory factors. The cytokines adipokine, IL6, TNF alfa, and C-reactive protein are elevated in the plasma of obese patients and have been associated with alteration of cartilage homeostasis and degeneration. During ambulation, the knee joint has to support 3–5 times the body weight, hence small changes in weight represent the high variation of forces to the joint. Regardless of the used method (bariatric surgery vs lifestyles modifications), there is around 10% risk reduction of knee OA per kilogram of body-weight decreased (same proportion applies in the opposite direction for the increase in weight).[35]

Regarding other non-pharmacological interventions, patients might benefit from thermal modalities, but there is insufficient evidence to recommend the use of transcutaneous electrical nerve stimulation (TENS) or therapeutic ultrasound."[36]

Table 2: Different exercise modalities for knee OA

Aerobic/endurance	**Exercise modalities** **Resistance/strength training**	**Balance/proprioceptive**	**Stretching**
Include activities like walking, climbing stairs, and cycling. They can decrease joint tenderness while improving functional status and respiratory capacity. Cycling is especially attractive to patients given the low impact profile. One study showed a reduction of 10–12% on the physical disability and the knee pain questionnaires.	Isometric, isotonic, isokinetic, and dynamic modalities have been studied. Most of them targeting quadriceps, hip abductors, hamstrings, and calf muscles. They improve strength, physical function, and pain levels, with similar efficacy and outcomes than aerobic exercises.	This includes modalities such as Tai Chi, using slow and gentle movements to adopt different weight baring postures while using breathing techniques.	This group will specifically help with patient's range of motion and flexibility.

Pharmacological management

Elderly people make up the great majority of OA patients, and the majority of them will have other comorbidities. The potential interactions and side effects that systemic drugs may cause in this population should therefore get particular attention. Acetaminophen and NSAIDs are examples of cyclooxygenase inhibitors, which have historically been the most widely used drugs. However, these drugs have limited long-term use due to their gastrointestinal, renal, cardiac, and haematological side effects. Some guidelines do not advocate paracetamol as an appropriate medical therapy strategy for moderate-to-severe OA because it has been demonstrated to be less effective than NSAIDs and not better than a placebo for pain control. [37] It has been demonstrated that topical NSAIDs are safer than systemic NSAIDs and have similar, if not slightly lower, efficacy. In brief follow-up studies, they were found to be more effective than a placebo at reducing pain during the first week of treatment, but beyond two weeks, no improvement was observed. [38]

The negative effects of long-term opiate use have come to light more and more recently. Additionally, research continues to show that opioids are not better than NSAIDs at reducing OA pain or WOMAC scores, and that there are far more hazards associated with using them than advantages. [39] "Tramadol, a serotonin and norepinephrine reuptake inhibitor with mild μ opioid receptor agonist characteristics, has demonstrated some value in treating severe and moderate OA if a patient is not responding to other treatments and the usage of an opioid is taken into consideration. This drug has a marginally lower risk of abuse potential and respiratory depression than other opioids." [40]

The US Food and Drug Administration (FDA) has approved duloxetine, a serotonin and norepinephrine reuptake inhibitor, to treat fibromyalgia and diabetic peripheral neuropathy. According to recent research, this drug works better than a placebo at reducing pain and enhancing function in OA patients when taken for longer than ten weeks.[41]

Interventional management

Intra-articular (IA) injections of various drugs have been investigated in the past. This is based on the theory that local therapies will have fewer negative systemic effects and that the medicine will act more directly inside the joint. "IA therapies are often more successful than NSAIDs and other systemic pharmacologic treatments, according to studies, but they also revealed that a portion of this benefit may be secondary to the IA placebo effect."[42]

Corticoid injections

By directly targeting nuclear receptors, corticoids (CS) block the inflammatory cascade on several levels and produce their immunosuppressive and anti-inflammatory actions. They are thought to be among the mechanisms of pain alleviation and increased joint mobility in knee OA because they reduce the activity and generation of metalloproteinases, prostaglandins, leukotrienes, and IL-1.

"Methylprednisolone Acetate (MA), Triamcinolone Acetate (TA), Triamcinolone Hexacetonide (TH), Betamethasone Acetate (BA), Beta-methasone Sodium Phosphate (BSP), and Dexamethasone are the FDA-approved Immediate Release (IR) corticosteroids currently available for IA use. [43] There have been previous attempts to determine which choice is the best. In contrast to the brief pain relief of 2-4 weeks observed with lower dosages, dosages equal to or more than 50 mg of prednisone (equivalent to 40 mg of TA and MA) appear to be associated with a longer pain reduction effect of 12-24 weeks." Although there may be some variations in the approved IR corticosteroid formulations' ability to reduce pain, the available data is inconclusive.[44]

Previous attempts have been made to identify suitable candidates. One of the first hypotheses was that individuals with knee effusion, synovitis, and increased synovial membrane thickness (as indicated by ultrasonography) would benefit the most from the anti-inflammatory properties.

Other potential factors, such as the level of knee tenderness, baseline pain, gender, BMI, and anxiety or depression, have not demonstrated any discernible predictive power.

In contrast to patients with severe radiographic alterations (3–4), those with a low degree of

radiographic abnormalities on the KL system (0–1) appear to respond better.

Several IA knee injection procedures have been previously described, including the mid-lateral and superolateral approaches (done with the knee extended), as well as the anterolateral and anteromedial techniques (administered with the knee flexed 60 to 90 degrees). According to studies, the best probability of accurately injecting the CS inside the knee joint is to use ultrasonic guidance in conjunction with the superolateral technique. The average accuracy while utilising ultrasound is 96.7%, compared to 81% when using landmarks. Additionally, when compared to other methods, effective utilisation of the ultrasound guidance can result in improved pain alleviation.

Complications are a worry for the use of this therapy even if they are uncommon (about 1 in 3000). Within the first three days, you may notice a self-limiting facial flush and temporary flare-ups from the pot injection.[45]

Extended-release triamcinolone acetonide

A chemical known as FX006 was created and authorised by the FDA before the end of 2017 in an effort to reduce side effects and prolong the pain reduction benefit while avoiding the high peak plasma concentrations associated with IR use. TA in FX006 is enclosed in microspheres, which range in size from 20 to 100 μm. The biocompatible substance Poly-Lactic-Co-glycolic Acid (PLGA), which makes up these microspheres, eventually breaks down into carbon dioxide and water.[46]

Non-corticoid interventional therapies[45]

In recent years, novel medicines and therapies that target components other than inflammation have been used as an alternative to the IA CS. Despite the potential nature of these products, further research is necessary to ascertain their safety profile, effectiveness, and applicability.

Hyaluronic acid addition by viscosupplementation

Type B synovial cells, fibroblasts, and chondrocytes produce hyaluronic acid (HA), a naturally

occurring glycosaminoglycan that is released into the synovial fluid. In addition to its remarkable absorption qualities and viscous lubrication, it may also have anti-inflammatory and antioxidant properties. Some suggested viscosupplementing the joint to try to restore the benefits of HA because the concentration and molecular weight of HA decline significantly in osteoarthritic knees. There is now conflicting evidence regarding efficacy, which leads to differences in the societies' recommendations. The OARSI has a "uncertain recommendation," the ACR has no recommendations on it, the AAOS does not advise using it, and a recent European consensus found that HA was both helpful and well tolerated for low and moderate grade OA. Finally, younger patients with lower KL scores and more severe knee pain may benefit more from this treatment.

Regenerative medicine

IA injections of autologous conditioned serum (ACS), platelet rich plasma (PRP), and mesenchymal stem cells (MSC) have been tested with the goal of halting and reversing the deterioration linked to OA. Their methods of action include reducing cytokine-mediated inflammatory responses and promoting anabolism and chondrocyte differentiation through the use of growth factors and stem cells. According to some studies, these techniques are safe, well-tolerated, and, in certain situations, better than HA and IA placebo in terms of knee function and pain reduction. To define and standardise the best practices for these goods' production, storage, and retrieval, additional study is needed in this still-emerging subject. [47]

PLATELET-RICH PLASMA

History of platelet-rich plasma

While platelet rich plasma (PRP) has higher platelet concentrations than baseline when compared to the same amount of whole blood, normal platelet counts in blood range from roughly 1,50,000 to 4,50,000/cum3.

One of the most promising therapeutic agents in regenerative medicine at the moment is platelet-rich plasma (PRP), which has a therapeutic value comparable to that of stem cells. It is being used more and more in orthopaedics, sports medicine, surgery, and aesthetic dermatology, among other medical specialities.

To aid in wound healing, physicians employed embryonic "extracts" made of cytokines and growth factors in the early 1940s. [48] The outcome of surgical procedures depends on the wounds healing quickly and efficiently. Thus, thrombin and fibrin were combined in skin grafting by Eugen Cronkite et al. [49] In this kind of surgery, the employment of the aforementioned components ensures that the flaps adhere firmly and steadily.

The typical platelet concentrate for transfusion was initially referred to as "platelet-rich plasma" by Kingsley et al. in 1954. [50] The first blood bank PRP preparations were made in the 1960s, and they gained popularity in the 1970s. [51]

The "EDTA Platelet Pack" was utilised in the late 1950s and early 1960s. The package included a plastic bag containing EDTA blood and enabled centrifugation to concentrate platelets that were still suspended in a tiny volume of plasma following the operation. [52]

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The "EDTA Platelet Pack" was utilised in the late 1950s and early 1960s. The package included a plastic bag containing EDTA blood and enabled centrifugation to concentrate platelets that were still suspended in a tiny volume of plasma following the operation.

Growth factors (GFs) were thought to be additional PRP chemicals produced by platelets that contributed to its effect. In the 1980s, the idea was validated. In order to heal damaged tissue, including skin ulcers, it was shown that platelets secreted bioactive chemicals (GFs). Numerous investigations of this matter have been carried out thus far. The combination of PRP and hyaluronic acid is one of the most researched topics in this area. Cohen made the discovery of epidermal growth factor (EGF) in 1962. Additional growth factors were vascular endothelial growth factor (VEGF) in 1989 and platelet-derived growth factor (PDGF) in 1974. [52]
The first researchers to describe platelet concentrate methods and call them autologous platelet-derived wound healing factors (PDWHF) were Knighton et al. in 1986. The use of these procedures in aesthetic medicine has grown since the protocols were developed. PRP has been utilised in regenerative medicine since the late 1980s.[52]

The Role of Platelets[53]

First to reach the site of tissue damage, platelets are especially active during the early inflammatory stages of the healing process. "Through cell membrane adherence, aggregation, clot formation, and the release of chemicals that aid in tissue repair and affect the reactivity of blood arteries and blood cell types involved in angiogenesis and inflammation, they contribute to homeostasis." Through degranulation, platelets mediate these effects by releasing vascular endothelial GF (VEGF), platelet-derived GF (PDGF), transforming GF-β1 (TGF-β1), basic fibroblastic GF (bFGF), and epidermal GF (EGF) from alpha granules (Table 3). Additionally, platelets contain membrane glycoproteins, metalloproteases, coagulation factors, and antibacterial and fungicidal proteins that may affect inflammation by triggering the production of additional integrins, interleukins, and chemokines. ADP, ATP, calcium ions, histamine, serotonin, and dopamine are all stored and released by the dense granules in platelets. These substances are involved in tissue regulation and regeneration. Within ten minutes of coming into touch with clotting cascade factors (like thrombin) or, in their absence, the exposed basement membrane,

platelet degranulation starts. Although GF secretion continues during the seven-day period of platelet viability, the majority of it happens within the first hour.

PDGF and TGF-β1 seem to be two of the more important modulators, even though many GFs are linked to wound healing. Early wound healing (during the acid tide) is facilitated by PDGF activation. According to in vitro research, platelet concentrate lysate exhibits higher PDGF concentrations and a greater ability to promote fibroblast proliferation at lower pH values (5.0). TGF-β stimulates fibroblasts to produce more collagen. Neutral or alkaline pHs, which correlate to the later stages of healing, boost its release (in vitro). By controlling macrophages' production of interleukin-1, PRP may prevent excessive early inflammation that could result in the creation of thick scar tissue.

The capacity of insulinlike GF-I (IGF-I) to promote the growth, differentiation, and hypertrophy of many cell lines has also been the subject of much research. Comparing the quantities of PDGF, VEGF, TGF-β1, and EGF in PRP to those in whole blood, separate investigations of GFs in PRP have revealed notable increases. Regarding IGF-I, there are contradictory findings; most research found that PRP did not raise IGF-I levels when compared to whole blood. Regarding the relationship between the GF content and platelet counts in PRP, there are also contradictory findings. Although the exact cause of these discrepancies is unknown, it may have something to do with variations in the patient's age, health, or platelet count. Alternately, variations in GF content and platelet count could result from different sample handling, processing, and storage techniques in addition to the kind of assay used. When evaluating and contrasting PRP generation techniques and results, it is important to consider the variety of PRP products. .

PRP in Orthopaedics

"The potential delivery of a physiologically natural balance or ratio of GFs and other cytokines with anabolic and catabolic functions in supraphysiologic concentrations directly into the site of injury to potentially optimise the healing environment is what makes PRP so appealing when used to treat soft tissue injuries." Theoretically, preserving a natural ratio of GFs could support the homeostatic milieu of the body and offer a wealth of healing factors without interfering with their in vivo interactions. Its availability, affordability, ease of use, and lack of serious negative effects are equally alluring. Because PRP is autologous, there is little chance of immunological rejection or disease transmission. There is a dearth of well-conducted randomised controlled clinical trials in spite of this almost intuitive and immense potential.

Devices for producing PRP are commercially available from a number of manufacturers." The amount of whole blood, the use of an anticoagulant (acid citrate dextrose), the centrifugation time and speed, the final volume, and the number of platelets in the platelet concentrate are all different depending on the method utilised to create the platelet concentrate products". Additionally, the application can differ based on whether thrombin is used to start the clotting cascade by degranulating platelets or bicarbonate is used to buffer the acidic character of PRP generated with acid citrate dextrose. The adhesive support that can confine the platelets and their GFs at the therapy location could be a potential benefit of administering PRP gel.

The American Red Cross states that PRP is at least 5.5 × 1010 platelets per 50 millilitres. When compared to whole blood, this results in a two- to seven-fold increase in platelet concentration. Between 150 000 to 450 000 platelets per μL of whole venous blood is the usual range for human platelet concentrations. "Between 2.5 to 8.0 times the concentration of platelets in whole blood, the concentrations of platelets in PRP vary greatly." Although there is a lack of strong scientific data, it is said that the therapeutic benefit of platelet concentrates is more predictable when this fourfold rise in platelet concentration is attained. Concentrates that fall below this threshold may still have clinical benefits.

PRP for Use in Cartilage Injuries and Early Osteoarthritis[53]

Numerous macro- or microtraumatic events commonly affect articular cartilage, which can cause a breakdown of tissue homeostasis, accelerate articular cartilage degradation, and eventually lead to arthritis. For orthopaedic surgeons, articular cartilage degeneration remains a difficult issue due to cartilage's intrinsically low ability for regeneration.

In order to modify the phenotypic expression of chondrocytes, GFs are essential. Through chondrogenic differentiation of mesenchymal stem cells, enhanced chondrocyte phenotypic expression and matrix production, and suppression of interleukin-1-mediated reduction in proteoglycan synthesis, TGF-β influences cartilage regeneration. PDGF promotes chondrocyte proliferation, up-regulates proteoglycan production, and aids in maintaining the hyaline-like chondrogenic phenotype. It has been demonstrated that IGF-I inhibits proteoglycan catabolism and promotes proteoglycan synthesis. Other GFs with chondroinductive functions include bFGF and VEGF. With the probable exception of IGF-I, all of these GFs are found in the α-granules of platelets and can be administered intra-articularly in large doses. PRP boosts matrix formation and chondrocyte proliferation in vitro, and research using animal models have shown that PRP injections stop osteoarthritis from progressing following ACL transection. PRP injections enhanced function and reduced pain in a clinical investigation of 100 individuals with degenerative cartilage lesions (determined by the Kellegren score method).

Table 3: Growth factors present in platelet-rich plasma.

Name	Acronym	Function
Platelet-derived growth factor	PDGF	Stimulates fibroblast production, chemotaxis, stimulates transforming growth factor–β1, collagen production, upregulation of proteoglycan synthesis
Transforming growth factor–β1	TGF-β1	Modulates proliferation of fibroblasts, formation of extracellular matrix, cell viability; increases production of collagen from fibroblasts, suppression interleukin 1–mediated effects on proteoglycan synthesis in cartilage
Basic fibroblastic growth factor	bFGF	Produces collagen; stimulates angiogenesis, proliferation of myoblasts
Vascular endothelial growth factor	VEGF	Promotes angiogenesis
Epidermal growth factor	EGF	Promotes cell differentiation, angiogenesis, proliferation of mesenchymal and epithelial cells

HYALURONIC ACID[54, 55]

A high molecular weight polymer, hyaluronic acid is extensively found in the extracellular matrix of connective tissue.

HA's physicochemical characteristics are classified as high (HMW), medium (MMW), or low (LMW) based on its spatial conformation and molecular mass. The biological effects that HA has on human tissues appear to be significantly influenced by its molecular weight. Generally speaking, MMW ranges from 800,000 to 2,000,000 Daltons (Da), HMW averages 6,000,000, while LMW HA ranges from 500,000 to 730,000 Da. Around 5 to 7 million Da of HA are found in healthy people's joints, while about 1 million Da is found in osteoarthritic joints. HMW HA molecules crosslink to create a very viscous fluid that acts as a lubricant and shock absorber. Furthermore, this kind of HA possesses qualities that promote cell development. The main non-protein component of synovial fluid, HA, forms a coating around cells. Whether synthetic or natural, it binds to cellular receptors and interacts with pro-inflammatory mediators to control gene expression, migration, and cell proliferation. Because HA is a strong collagen activator, particularly of type I collagen, it can aid in tissue healing and cellular integrity preservation. Because of these characteristics, HA is a very helpful orthobiologic tool for tendon and chondral tissue repair under a variety of conditions.

Indications

There are numerous hyaluronic acid formulations for numerous FDA-approved uses. Although there are numerous different ophthalmic and topical formulations available, the most popular application indications are for intra-articular usage and cosmetics.

Injectable hyaluronic acid gel fillers assist maintain a youthful appearance, improve facial contour, and replace volume lost as a result of ageing or illness. One of the most popular procedures in a dermatologist's cosmetic practice these days is filler injection. The concentration of hyaluronic acid, particle size, cross-linking density, duration, and presence of lidocaine vary throughout the many varieties of hyaluronic acid gel fillers. For deep dermal injections, high-density, large-

particle fillers are advised, whereas low-density, small-particle fillers are advised for fine lines. Because of its low allergic reaction, ease of injection, quick recovery, repeatability, and instantaneous results, hyaluronic acid filler has gained popularity. The glabella, nasolabial and melolabial folds, lips, perioral rhytids, infraorbital hollows, and chin are all common injection sites.

Hyaluronic acid intraarticular injections are also frequently utilised, particularly to relieve pain in individuals with osteoarthritis of the knees. Because most clinicians are concerned about recurring intraarticular corticosteroid injections, they have gained popularity as a non-surgical therapy option. There are other preparations available, such as different commercially available injections of hylan polymers A and B, hyaluronan, and sodium hyaluronate.

"United States Food and Drug Administration (FDA) Labeled Indications"

Intraarticular injection:

• "To relieve pain in individuals with mild to moderate knee osteoarthritis (OA) who have not responded to analgesics or conservative non-pharmacological treatments. No other joints have been examined or approved by the FDA for this treatment."

Mechanism of Action

"A naturally occurring substance, hyaluronic acid is a glycosaminoglycan polymer made up of alternating residues of the monosaccharides N-acetyl-d-glucosamine and d-glucuronic acid that combine to create a linear polysaccharide chain. All organisms have hyaluronic acid in its pure form; it is not species- or tissue-specific. Thus, in theory, hyaluronic acid shouldn't trigger an immunological reaction.

"A major component of the extracellular matrix, hyaluronic acid is present in many human tissues, including the skin, eyes, connective tissue, and synovium." The extremely anionic properties of hyaluronic acid allow it to draw in water, which causes swelling, volume creation, and structural support. Collagen and hyaluronic acid production in the skin decline with age. Overlying wrinkles appear when the skin's viscoelastic qualities are lost. Dermal fillers containing hyaluronic acid

replace lost volume to prevent ageing. Furthermore, it has been demonstrated that hyaluronic acid fillers alter fibroblast morphology and boost collagen synthesis.

There are two types of hyaluronic acid fillers: animal-derived and non-animal-derived. Animal-derived fillers are made from rooster combs, while Streptococcus biofermentation produces non-animal-derived hyaluronic acid. Depending on whether it is manufactured using particle or non-particulate processes, the hyaluronic acid filler can be further categorised. “While the longevity of non-particulate created hyaluronic acid filler is determined by cross-linking density, the longevity of particle manufactured hyaluronic acid filler is determined by particulate size.”

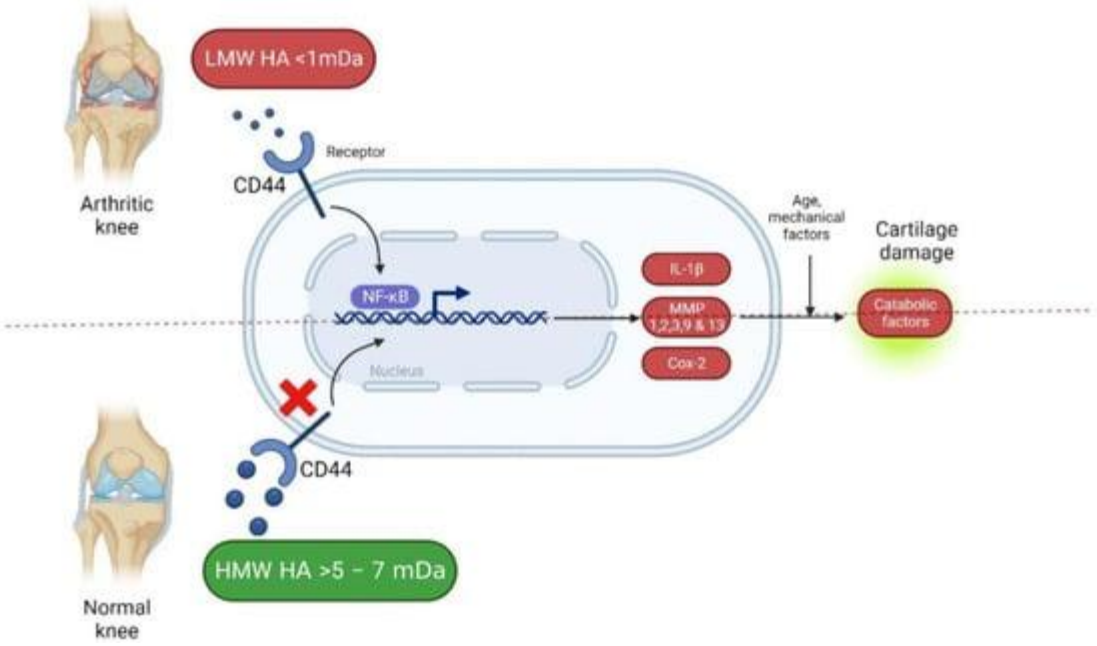
The cross-linked modified hyaluronic acid particles in the hyaluronic acid filler enable the creation of a more concentrated hyaluronic acid with increased resistance to physical and chemical deterioration. Water gradually replaces the hyaluronic acid filler as it breaks down and degrades, producing a less concentrated hyaluronic gel that yet has the same volume. We call this process "isovolumetric degradation." Depending on the region, the kind of filler used, and the injection technique, the benefits of hyaluronic acid filler might last anywhere from four to six months.

When applied intra-articularly, hyaluronic acid works in a similar way. Natural hyaluronic acid is found in cartilage and synovial fluid. In osteoarthritis, hyaluronic acid concentrations drop along with the size of individual hyaluronic acid molecules, which lowers the viscosity of the synovial fluid. With half-lives varying from 17 hours to 1.5 days, hyaluronic acid is eliminated from the joint after injection in a matter of hours. Large molecular weight hyaluronic acid formulations, whether synthesised or purified, have a longer half-life.

The clinical effect, which includes pain alleviation from intraarticular hyaluronic injections, lasts for several months despite the short half-life. The sustained effectiveness of intraarticular hyaluronic acid injections has been attributed to a number of causes. The natural synovial sites that generate hyaluronic acid may be stimulated by hyaluronic acid injection. Additionally, hyaluronic acid has been shown to have anti-inflammatory and anti-nociceptive properties. With differing outcomes, a number of meta-analyses have been conducted to assess the effectiveness of various

hyaluronic acid formulations for the treatment of osteoarthritis. Most people agree that a series of intraarticular hyaluronic acid injections causes minor but noticeable symptoms that continue for a long time.

Figure 5: Hyaluronic acid in arthritis knees



Administration

The brand that is selected determines the concentration of the hyaluronic acid filler, which comes in preloaded syringes of different sizes. Any makeup should be removed, and the area should be cleaned with an antiseptic (usually chlorhexidine or isopropyl alcohol). To avoid biofilm, the procedure should be as aseptic as feasible. Topical or injectable anaesthetics, nerve blocks, cooling packs, and distraction tactics can all help reduce injection site pain. Using fanning, cross-hatching, linear threading, and serial puncture, the hyaluronic acid filler is injected into the mid to deep dermis. The injection site and the particular issue being addressed determine the approach to be employed. An injection into the submucosa is necessary for lip augmentation. Lips, glabellar lines, nasolabial folds, and periorbital and generalised face wrinkles are frequently the sites of injections. After the injections are finished, the patient should be instructed not to move the treatment region and should have a cool ice pack used to reduce swelling and bruises.

When given intraarticularly, the injection is made right into the knee's joint space. If there is a joint effusion, aspiration is advised. During administration, strict aseptic approach is required. Prior to the intra-articular injection of hyaluronic acid, a lidocaine or other local anaesthetic injection may be administered. For at least 48 hours following the injection, the patient should avoid strenuous or extended weight-bearing exercise. “The number of injections in each series, molecular weight, origin (bacterial or avian), viscosity, and presence or lack of cross-linkage vary among the various preparations that are available.”

Adverse effects

Intra-articular hyaluronic acid injections typically have minor side effects that go away on their own. The most frequent adverse effects include discomfort or reactivity at the local injection site. A post-injection flare, which is typically self-limited and can be resolved with rest, icing, and anti-inflammatory drugs, can occur in up to 2% of patients and manifest as increased pain, swelling, redness, and warmth. In these situations, aseptic fluid devoid of crystals is revealed by synovial fluid analysis. Intra-articular infections are exceedingly uncommon in clinical practice and have not been documented in clinical trials. There have been reports of hypersensitivity responses, such as angioedema and anaphylaxis. About 2% of patients in clinical trials have experienced systemic side effects, including rash, arthralgia, myalgia, cramping in the muscles, and nausea.

ADMINISTRATION OF INTRA ARTICULAR INJECTION FOR KNEE

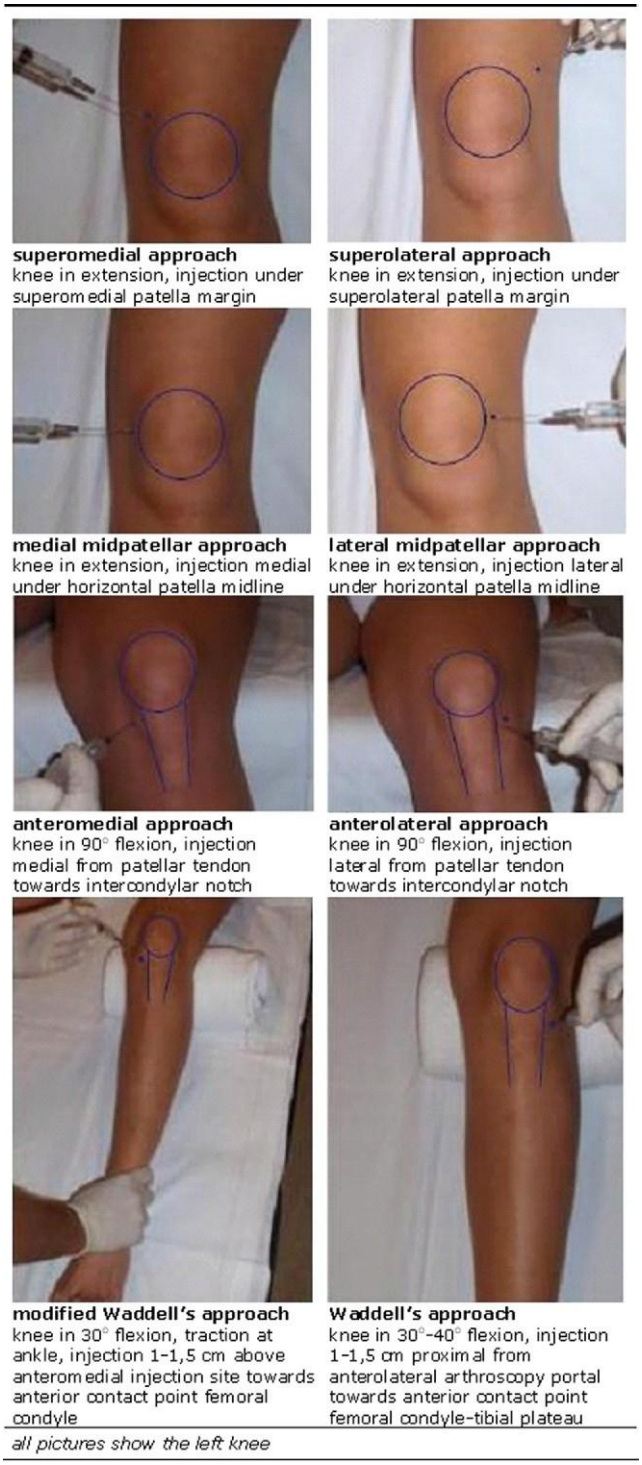


Figure 7 : different routes for administration of intra articular injection for knee

REVIEW OF RELATED STUDIES

Shahid A et al (2023)[56] This study aimed to determine if PRP injections administered in patients with knee OA over a six to eight-week time period demonstrated any benefit. The third injection showed a reduction in total WOMAC score, pain, stiffness, and physical function by 16.36%, 16.37%, 5.12%, and 18.03%, respectively. However, all scores returned close to baseline at the sixth-week follow-up post treatment. Results showed a trend of reduction in the WOMAC score. However, they are overall indicative of a placebo effect from the injections. Further studies are needed to explore whether the grade of OA and patients' weight have a significant impact on the results.

Vetrivel C. Sengodan et al.[57] conducted a study on 256 participants in 2022 titled "Efficacy of Single Intra-Articular Injection of Hyaluronic Acid for Osteoarthritis of the Knee Joint in South Indian Population" and found that the WOMAC score significantly improved with a single dose of hyaluronic acid in the early stages of osteoarthritis.

Moretti L et al (2022)[58] The aim of this prospective study was to evaluate the efficacy and safety of Platelet Rich Plasma (PRP) injections in patients affected by knee osteoarthritis (KOA). A statistically significant VAS, KSS and WOMAC reduction emerged in the comparison between evaluations ($p < 0.05$), MRI demonstrated non-statistically significant improvement in cartilage thickness for both tibial plate and femoral plate ($p = 0.46$ and $p = 0.33$ respectively), and no radiographic changes could be seen in any patients. They concluded that PRP injection represents a valid conservative treatment to reduce pain, improve quality of life and functional scores even at midterm of 6 months follow-up.

In a study on the relative effectiveness of intra-articular injections in the treatment of knee osteoarthritis conducted in 2021 by **Singh H, Knapik DM, et al.,** it was found that PRP produced better results than PRGF, HA, CS, and placebo for the treatment of symptomatic knee OA at a minimum 6-month follow-up.[59]

on 58 subjects, **Wu Q et al.**[60] conducted a meta-analysis study in 2020 comparing the

effects of platelet-rich plasma and hyaluronic acid on knee osteoarthritis pain relief. They came to the conclusion that there was no significant difference between the two treatments.

Belk JW et al (2021)[61] systematically reviewed the literature to compare the efficacy and safety of PRP and HA injections for the treatment of knee OA. They concluded that patients undergoing treatment for knee OA with PRP can be expected to experience improved clinical outcomes when compared with HA. Additionally, leukocyte-poor PRP may be a superior line of treatment for knee OA over leukocyte-rich PRP, although further studies are needed that directly compare leukocyte content in PRP injections for treatment of knee OA.

Tang JZ et al (2020)[62] This study aimed to evaluate the clinical efficacy of platelet-rich plasma (PRP) injection compared with hyaluronic acid (HA) injection for patients undergoing knee osteoarthritis. They concluded that Intra-articular PRP injection appeared to be more efficacious than HA injection for the treatment of KOA in terms of short-term functional recovery. Moreover, PRP injection was superior to HA injection in terms of long-term pain relief and function improvement. In addition, PRP injection did not increase the risk of adverse events compared to HA injection.

A 2019 study by **Guillibert C et al.** on 60 patients with knee osteoarthritis found that a single large volume injection of autologous pure PRP significantly improved the condition.[63]

2019 study of "a prospective randomised controlled study" by **Huang Y et al.** on the use of intra-articular injections of platelet-rich plasma, hyaluronic acid, or corticosteroids in the treatment of knee osteoarthritis. This study found that intra-articular PRP injection in the early stages of knee osteoarthritis significantly reduced pain and improved clinical outcomes.[64]

A study on the effectiveness of platelet-rich plasma treatment in treating knee osteoarthritis and its dependence on the degree of cartilage destruction was conducted in 2019 by **Burchard R et al.** This study found that regardless of the degree of cartilage loss, intra-articular injection of PRP decreases pain in individuals with osteoarthritis of the knee joint and improves osteoarthritis symptoms.[65]

There was no significant difference between the intra-articular PRP group and the hyaluronic acid injection group in the KOOS score, but there was a significant difference in the VAS, WOMAC, and IKDC scoring favouring PRP over hyaluronic acid injection in the treatment of osteoarthritis. This study was conducted in 2018 by **Zhang HF et al.** on 1062 subjects.[66]

In 2018, **Magalon J, Jouve E, et al.** conducted a "randomised double blind study" on Growth factors levels to determine the efficacy of intra-articular hyaluronic acid injection versus platelets rich plasma in treating knee osteoarthritis. They came to the conclusion that the latter had better results after three months for WOMAC and VAS scores.[67]

MATERIAL AND METHODS

- **Study design:** Randomized Control Trial
- **Study area:** Department of Orthopedics, BLDE (deemed to be university) Shri B.M. Patil's Medical College, Hospital and Research Centre, Vijayapura, India.
- **Study period:** Research study was conducted from March 2023 to March 2024. Below is the work plan.

Table 1: Work plan of the study with percentage of allocation of study time and duration in months

Work plan	% of allocation of study time	Duration in months
Understanding the problem, preparation of questionnaire	5-10%	March 2023 to June 2023
Pilot study, Validation of questionnaire, data collectio and manipulation	Upto 80%	July 2023 to September 2024
Analysis and interpretation	5-10%	October 2024 to December 2024
Dissertation write-up and submission	5-10%	January 2025 to March 2025

- **Sample size**: The anticipated Mean±SD of IKDC baseline in PRP 36.6±10.4 and in hyalouronic acid patients 30.0±8.8 resp. the required minimum sample size is 35 per group (i.e. a total sample size of 70, assuming equal group sizes) to achieve a power of 80% and a level of significance of 5% (two sided), for detecting a true difference in means between two groups.

$$N = 2\left[\frac{(Z_{\alpha}+z_{\beta})*S}{d}\right]^2$$

$Z\propto$: Level of significance=95%

$z\beta$: Power of the study=80%

d=clinically significant difference between two parameters

SD= Common standard deviation

- **Inclusion criteria:**

1. Patients who are 40 years or older
2. Clinical assessment and confirmation of osteoarthritic changes with radiography.
3. Grades 1 and 2 of osteoarthritis (Kellgren- Lawrence grade)
4. Patients who are willing to get treatment and provide signed, informed permission

- **Exclusion criteria:**

1. . Infection or injury near the injection site
2. Knee osteoarthritis (Kellgren- Lawrence grade 3 & 4)
3. Uncontrolled type 2 diabetes

METHODOLOGY

The study was conducted at the Department of Orthopedics OPD in BLDE (Deemed to be University) Shri B.M.Patil Medical College, Hospital and Research Centre, Vijayapura. Patients with knee osteoarthritis were diagnosed through comprehensive clinical examination, detailed history taking, and radiological examination using X-rays.

Prior to the interventions, all patients underwent standard pre-procedure investigations including complete blood count, random blood sugar testing, screening for HIV, HBsAg, and HCV, and knee X-rays. Additional specific investigations were conducted as needed based on individual patient requirements.

For the PRP preparation, approximately 50 ml of patient blood was drawn into a 60-ml syringe pre-filled with 5 ml of sodium citrate. The collected blood was centrifuged using a desk-top centrifuge at 3,000 rotations per minute for 15 minutes. Following centrifugation, the platelet-poor plasma and platelet-rich plasma were isolated. The platelet-poor plasma was discarded, and the platelet-rich plasma underwent an additional agitation step. The final PRP concentrate achieved a platelet concentration approximately 6-8 times higher than baseline whole blood. The entire process from blood collection to injection took approximately 30-35 minutes.

For the hyaluronic acid group, a prefilled 2ml syringe containing 20mg of hyaluronic acid with a weight-average molecular weight of 0.6-1.5 Million Daltons was used.

The injection procedure was performed in a sterile outpatient setting. With the knee flexed at 30 degrees, injections were administered using a 22-gauge needle via the lateral suprapatellar approach. The PRP group received 5cc of platelet concentrate, while the hyaluronic acid group received 2cc of prefilled hyaluronic acid. The intraosseous puncture site was positioned 1 cm above the lateral tibial plateau and 1 cm lateral to the patellar tendon, with the needle directed toward the medial joint line of the knee. Both groups received injections at baseline, 1 month, and 2 months post-procedure.

Post-procedure management included analgesics and anti-inflammatory medications as needed, along with cold compression therapy applied to the knee for approximately 3 minutes. Patients were followed up clinically at 3 months and 6 months intervals. Treatment outcomes were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and Visual Analogue Scale (VAS).

VISUAL ANALOGUE SCORE

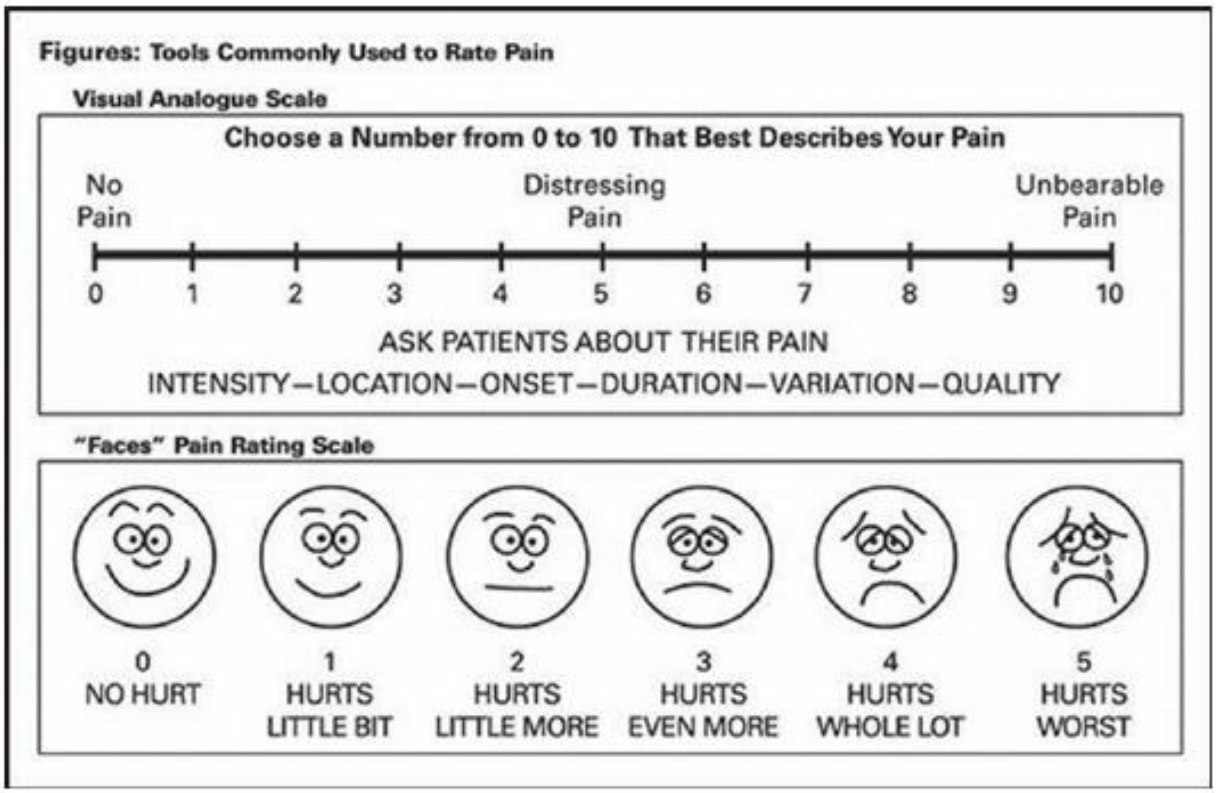


Figure 8: VAS SCORING SYSTEM

WOMAC SCORE

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Severity, on average, during the last 48 hours, of:

Pain

	None	Slight	Moderate	Severe	Extreme
Pain – Walking	☐	☐	☐	☐	☐
Pain – Stair climbing	☐	☐	☐	☐	☐
Pain – Nocturnal	☐	☐	☐	☐	☐
Pain – Rest	☐	☐	☐	☐	☐
Pain – Weightbearing	☐	☐	☐	☐	☐

Stiffness:

Morning Stiffness	☐	☐	☐	☐	☐
Stiffness occuring during the day	☐	☐	☐	☐	☐

Level of difficulty performing the following functions, on average, during the last 48 hours:

	None	Slight	Moderate	Severe	Extreme
Descending stairs	☐	☐	☐	☐	☐
Ascending stairs	☐	☐	☐	☐	☐
Rising from sitting	☐	☐	☐	☐	☐
Standing	☐	☐	☐	☐	☐
Bending to the floor	☐	☐	☐	☐	☐
Walking on flat	☐	☐	☐	☐	☐
Getting in/out of a car	☐	☐	☐	☐	☐
Going shopping	☐	☐	☐	☐	☐
Putting on socks	☐	☐	☐	☐	☐
Rising from bed	☐	☐	☐	☐	☐
Taking of socks	☐	☐	☐	☐	☐
Lying in bed	☐	☐	☐	☐	☐
Getting in/out of bath	☐	☐	☐	☐	☐
Sitting	☐	☐	☐	☐	☐
Getting on/off toilet	☐	☐	☐	☐	☐
Performing heavy domestic duties	☐	☐	☐	☐	☐
Performing light domestic duties	☐	☐	☐	☐	☐

The WOMAC parameters are:
0 – none, 1 – slight, 2 – moderate, 3 – severe, 4 – extreme.
The index is out of a total of 96 possible points, with 0 being the best and 96 being the worst

STATISTICAL ANALYSIS

Data was entered in excel sheet and analyzed using SPSS version 21. Results were presented in tabular and graphical forms Mean, median, standard deviation and ranges were calculated for quantitative data. Qualitative data were expressed in terms of frequency and percentages. Student t test (Two Tailed) was used to test the significance of mean and P value <0.05 was considered significant.

RESULTS

The present study was conducted in the department of Orthopedics at Shri B.M.Patil's Medical College, Hospital and Research Centre, Vijayapura from March 2023 to March 2025 to intra-articular platelet rich plasma vs hyaluronic acid in treatment of osteoarthritis of knee.

Total of 70 patients with 35 in each group.

- **Hyaluronic acid :**35 patients
- **Platelet rich plasma :**35 patients

Table 1: Comparison of age among groups

Age (in years)	Groups		p-value
	HA	PRP	
41-50	12 (34.3%	12 (34.3%)	0.68
51-60	9 (25.7%)	9 (25.7%)	
61-70	8 (22.9%)	11 (31.4%)	
71-80	6 (17.1%)	3 (8.6%)	
Total	**35 (100%**	**35 (100%)**	

Table 1 and graph1 shows the age distribution between the HA and PRP treatment groups. Both groups had identical percentages of patients in the 41-50 age range (34.3%) and 51-60 age range (25.7%). The PRP group had a slightly higher percentage of patients in the 61-70 age range (31.4% vs 22.9%), while the HA group had more patients in the 71-80 age range (17.1% vs 8.6%). With a p-value of 0.68, there was no statistically significant difference in age distribution between the two treatment groups, indicating they were well-matched by age.

Graph 1: Comparison of age among groups

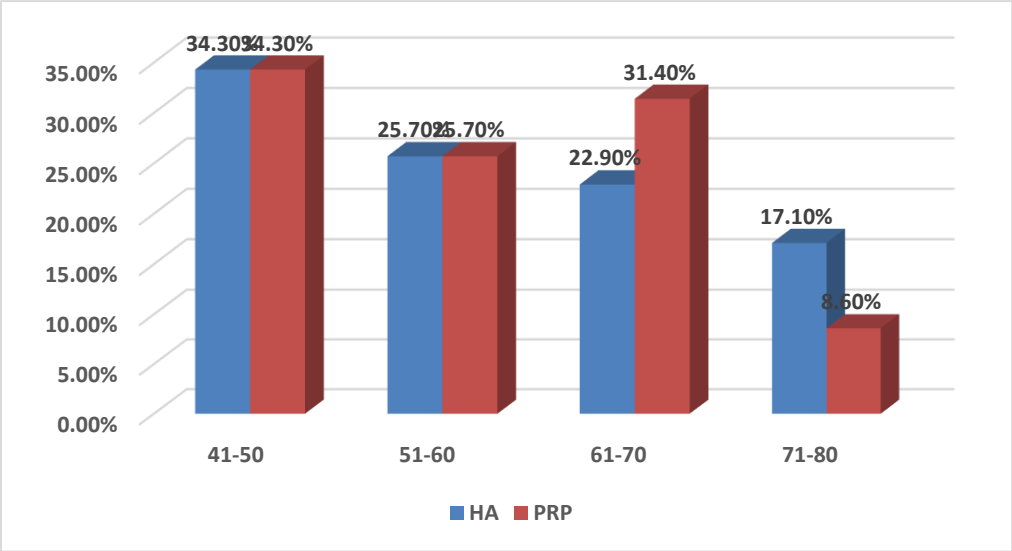


Table 2: Comparison of gender among groups

Gender	Groups		p-value
	HA	PRP	
Female	16 (45.7%	9 (25.7%)	0.08
Male	19 (54.3%	26 (74.3%	
Total	**35 (100%**	**35 (100%**	

Table 2 and graph 2 presents the gender distribution among the treatment groups. The HA group had a more balanced gender distribution with 45.7% female and 54.3% male patients, while the PRP group had a higher proportion of male patients (74.3%) compared to female patients (25.7%). However, with a p-value of 0.08, this difference was not statistically significant, though it approached the significance threshold of 0.05.

Graph 2: Comparison of gender among groups

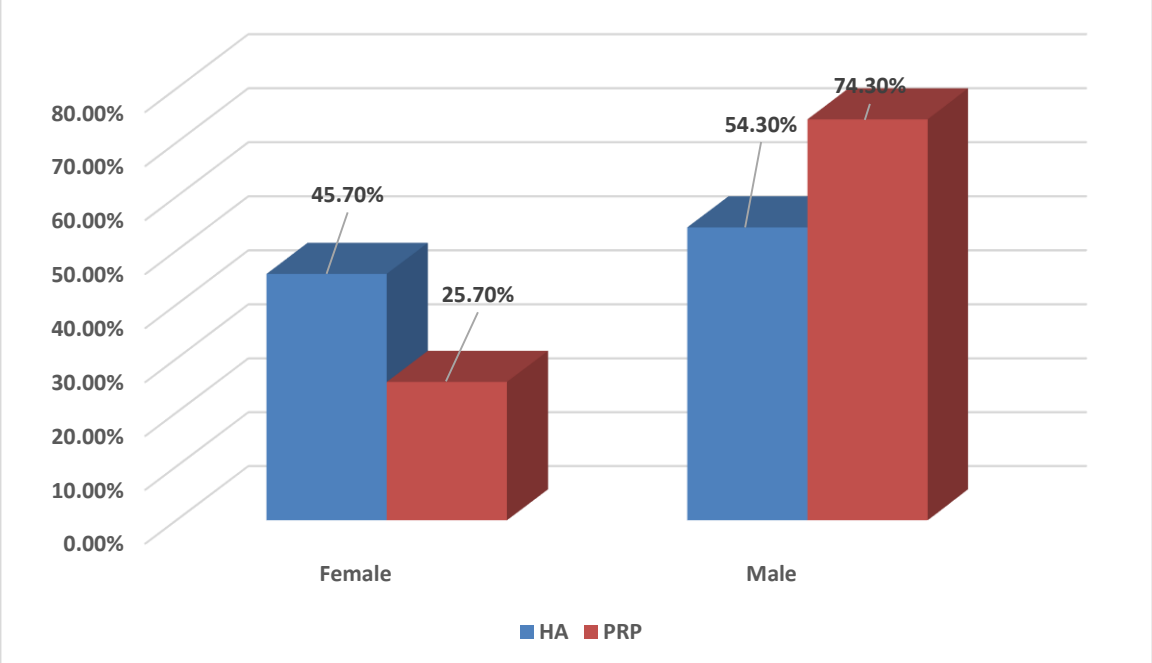


Table 3: Comparison of BMI among groups

BMI	Groups		p-value
	HA	PRP	
18.5-24.9	5 (14.3%)	6 (17.1%)	0.94
25-29.9	18 (51.4%	17 (48.6%	
>30	12 (34.3%	12 (34.3%	
Total	**35 (100%**	**35 (100%**	

Table 3 and graph 3 compares the Body Mass Index (BMI) distribution between the two groups. Both groups showed similar BMI distributions, with the majority of patients falling in the overweight category (25-29.9 BMI): 51.4% in the HA group and 48.6% in the PRP group. Both groups had identical percentages (34.3%) of obese patients (BMI >30). The p-value of 0.94 indicates that the BMI distribution was very similar between the two groups with no statistically significant difference.

Graph 3: Comparison of BMI among groups

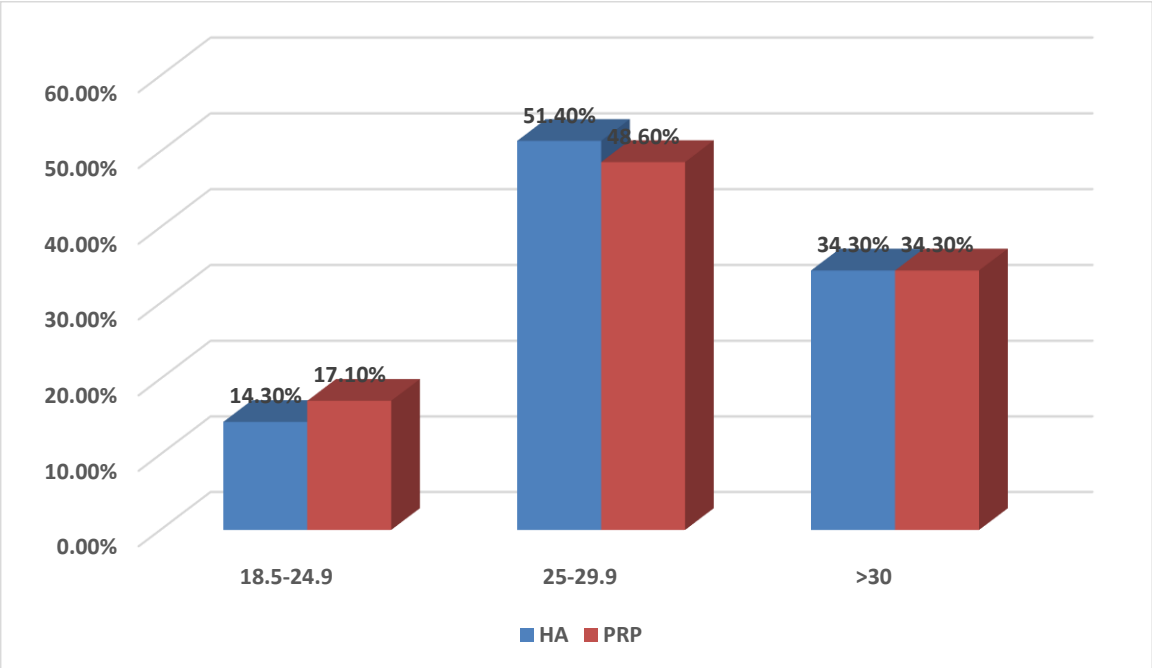


Table 4: Comparison of Kellgren Lawrence grade among groups

Kellgren Lawrence grade	Groups		p-value
	HA	PRP	
1	15 (42.9%	21 (60%	0.15
2	20 (57.1%	14 (40%	
Total	**35 (100%**	**35 (100%**	

Table 4 and graph 4 illustrates the distribution of Kellgren Lawrence grades, which measure the severity of knee osteoarthritis. The PRP group had more patients with grade 1 (milder) osteoarthritis (60%) compared to the HA group (42.9%), while the HA group had more patients with grade 2 osteoarthritis (57.1%) compared to the PRP group (40%). However, with a p-value of 0.15, this difference was not statistically significant.

Graph 4: Comparison of Kellgren Lawrence grade among groups

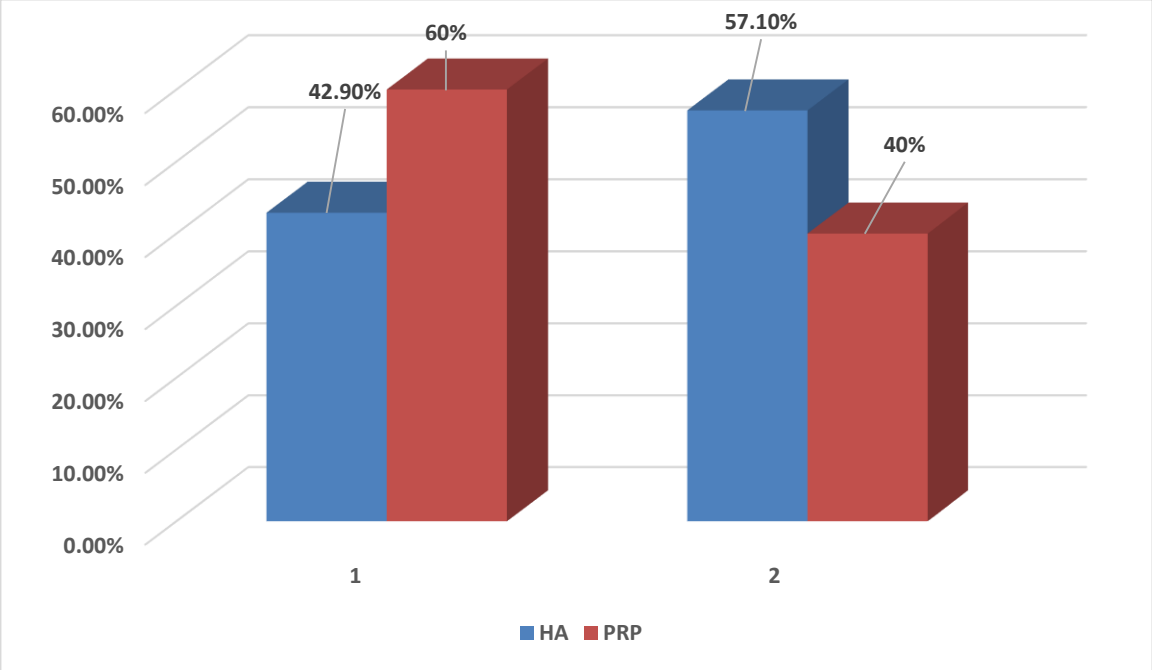


Table 5: Comparison of affected knee among groups

Affected knee	Groups		p-valu
	HA	PRP	
Left	16 (45.7%	17 (48.6%	0.55
Right	13 (37.1%	15 (42.9%	
Bilateral	6 (17.1%)	3 (8.6%)	
Total	**35 (100%**	**35 (100%**	

Table 5 and graph 5 shows the distribution of affected knees between the treatment groups. Both groups had similar distributions of left knee involvement (45.7% in HA vs 48.6% in PRP) and right knee involvement (37.1% in HA vs 42.9% in PRP). The HA group had a higher percentage of bilateral knee involvement (17.1%) compared to the PRP group (8.6%). With a p-value of 0.55, there was no statistically significant difference in the distribution of affected knees between the two groups.

Graph 5: Comparison of affected knee among groups

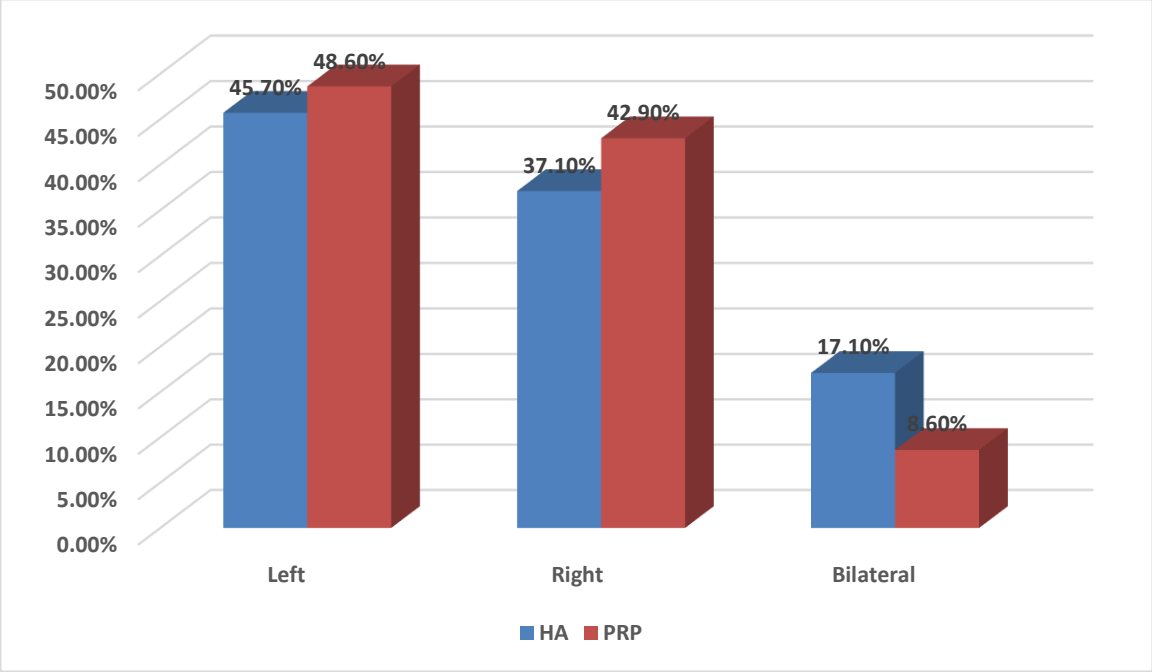


Table 6: Comparison of VAS at different intervals among groups

VAS (mean±SD)	Groups		p-value
	HA	PRP	
Baseline	6.5±0.81	6.5±0.8	0.84
3 months	3.12±0.48	4.65±0.68	**<0.001**
6 months	3.14±0.51	2.08±0.45	**<0.001**

Table 6 and graph 6 compares the Visual Analog Scale (VAS) pain scores between the groups at different time points. Both groups started with identical baseline pain scores (6.5±0.81 for HA and 6.5±0.8 for PRP). At 3 months, the HA group showed significantly better pain relief with a lower VAS score (3.12±0.48) compared to the PRP group (4.65±0.68). However, at 6 months, the PRP group demonstrated significantly better pain control (2.08±0.45) compared to the HA group (3.14±0.51). Both the 3-month and 6-month differences were statistically significant ($p<0.001$).

Graph 6: Comparison of VAS at different intervals among groups

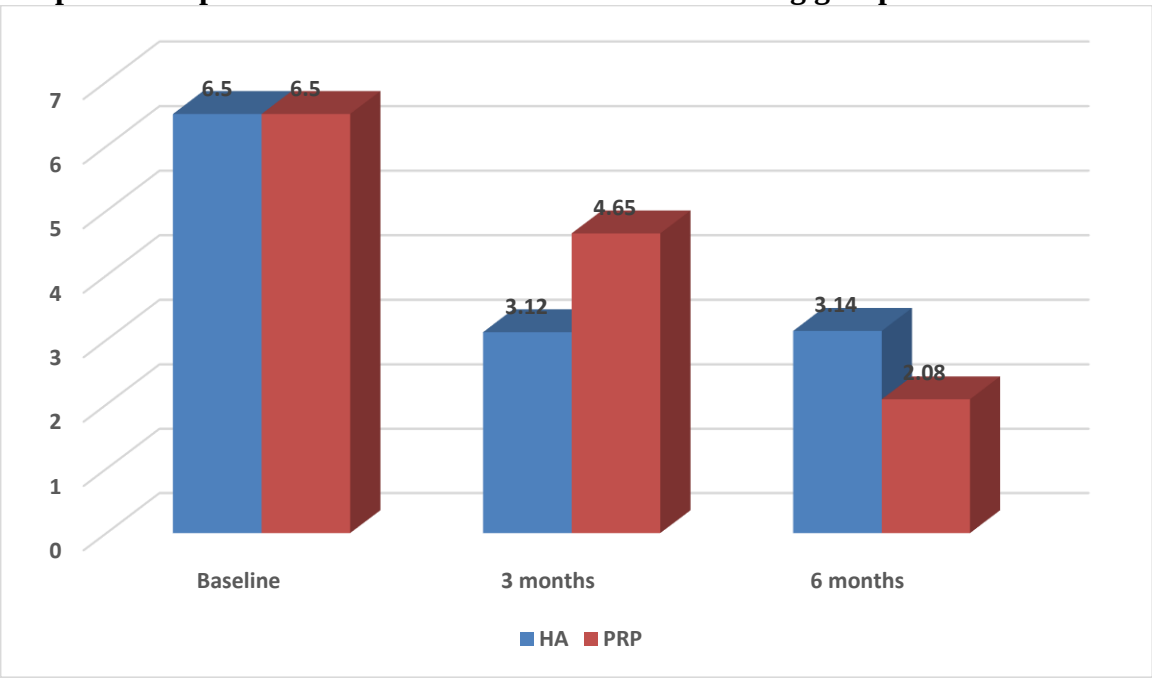


Table 7: Comparison of WOMAC scores at different intervals among groups

WOMAC scores (mean±SD)	Groups		p-value
	HA	PRP	
Baseline	67.4±6.4	68.2±6.4	0.55
3 months	31.7±4.3	47.2±5.4	**<0.001**
6 months	32.4±4.6	22.11±3.2	**<0.001**

Table 7 and graph 7 compares the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores between the groups. Both groups had similar baseline WOMAC scores (67.4±6.4 for HA and 68.2±6.4 for PRP). At 3 months, the HA group showed significantly better improvement with a lower WOMAC score (31.7±4.3) compared to the PRP group (47.2±5.4). However, at 6 months, the PRP group demonstrated significantly better results (22.11±3.2) compared to the HA group (32.4±4.6). Both the 3-month and 6-month differences were statistically significant (p<0.001).

Graph 7: Comparison of WOMAC scores at different intervals among groups

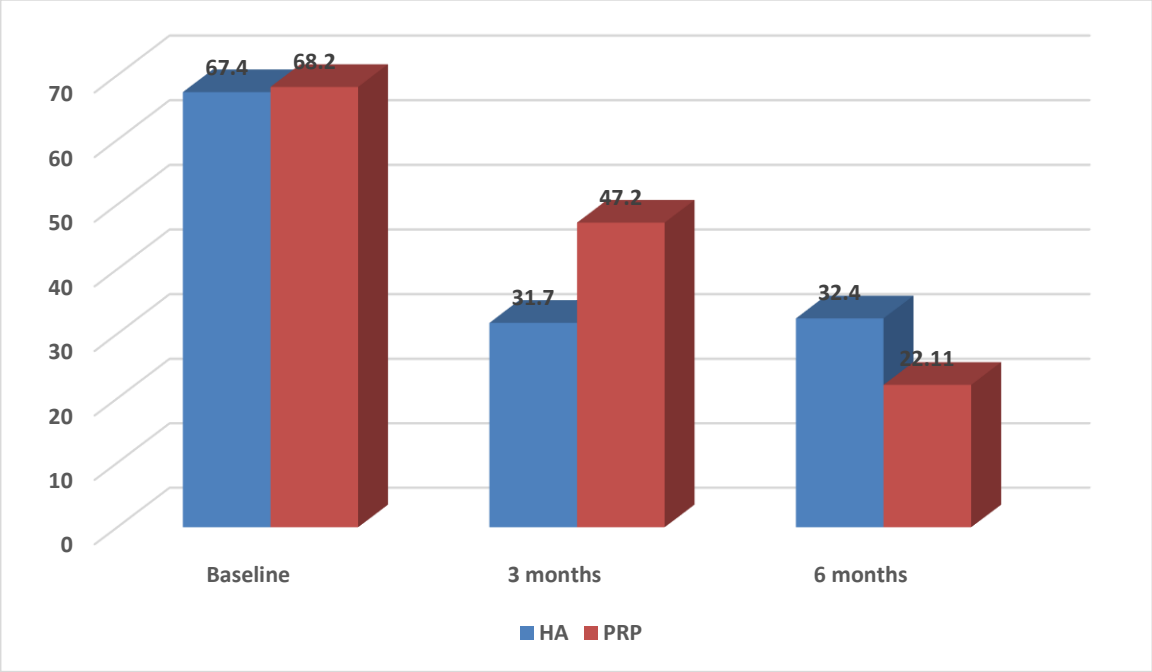
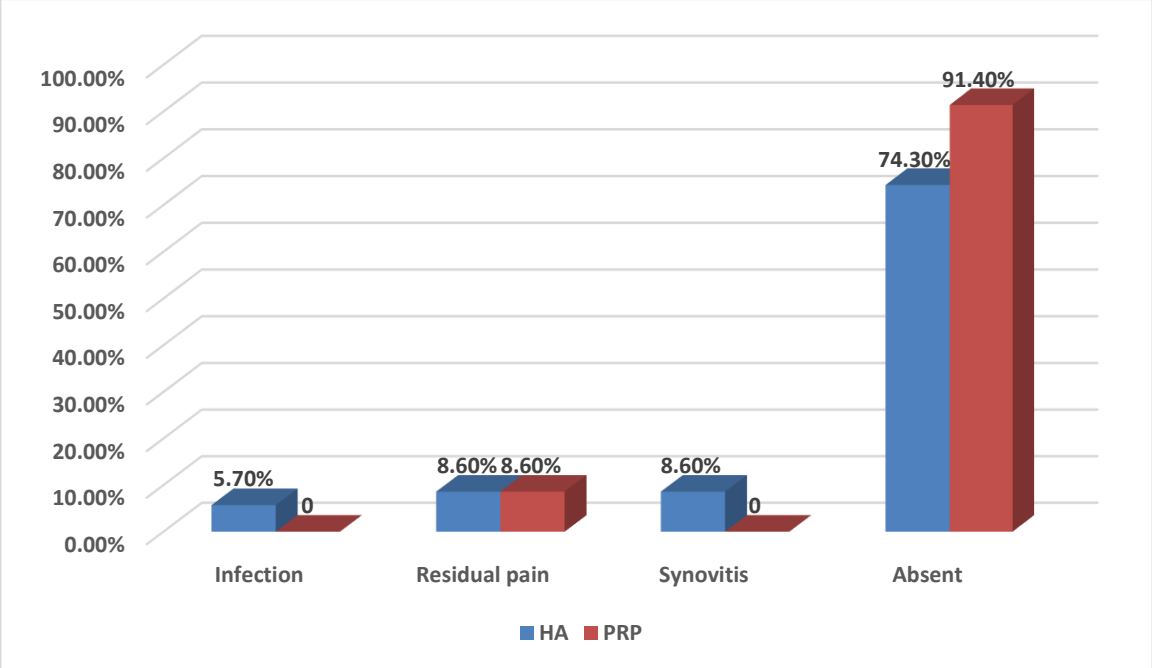


Table 8: Comparison of complications among groups

Complications	Groups		p-value
	HA	PRP	
Infection	2 (5.7%	0	0.13
Residual pain	3 (8.6%	3 (8.6%	
Synovitis	3 (8.6%	0	
Absent	26 (74.3%	32 (91.4%	
Total	**35 (100%**	**35 (100%**	

Table 8 and graph 8 compares complications between the treatment groups. The HA group experienced more complications overall with infection in 5.7% of patients, residual pain in 8.6%, and synovitis in 8.6%, while the PRP group only reported residual pain in 8.6% of patients with no cases of infection or synovitis. Overall, 91.4% of patients in the PRP group had no complications compared to 74.3% in the HA group. However, with a p-value of 0.13, this difference did not reach statistical significance.

Graph 8: Comparison of complications among groups



CASE REPRESENTATION

INTRA-ARTICULAR PRP INJECTION

CASE NO. : 1

NAME : GIRIMALAPPA

AGE/SEX : 55Y/M

O P NO : 52477

DATE OF INJECTION:

06/09/2023

OCCUPATION: FARMER

RESIDENCE : ATANI, BIJAPUR

Presenting complaints:

History of pain: C/O PAIN OVER RIGHT KNEE

a. Duration of pain
ONE YEAR

b. Nature of pain
GRADUALLY PROGRESSIVE EXAGERATED ON FLEXION AND WEIGHT BEARING

c. History of past medical disease

- Diabetes mellitus: NO
- Hypertension /IHD: NO

c. Personal and family history
NOTHING SIGNIFICANT

Examination

General physical examination

1. Built and nourishment
   a. BMI: 26.2

2. Signs
   Injection site redness , fever , chills:
   ABSENT

3. Vital parameters:

   Pulse : 88BPM

   BP : 130/90 mm hg

4. VAS SCORE : 6.4

5. WOMAC SCORE : 66

Systemic Examination
CVS : S1 AND S2 HEARD
NO MURMUR

RS : B/L NVBS PRESENT

P/A: SOFT NON TENDER

CNS: ALERT CONSCIOUS

Local Examination

(a) Inspection
DIFFUSE SWELLING OVER RIGHT KNEE

(b) Palpation

- Temperature : NO LOCAL RISE OF TEMOERATURE
- Tenderness : PRESENT OVER MEDIAL JOINT LINE
- Crepitus on range of movements ABSENT

TREATMENT

INTRA ARTICULAR INJECTION GIVEN : 4 ML

DOSE 1 ON 06/09/2023
DOSE 2 ON 08/10/2023
DOSE 3 ON 06/11/2023

INVESTIGATIONS

1. X-RAY KNEE STANDING AP LATERAL
   Osteophytes : PRESENT
   Decrease in joint space : PRESENT
   KELLGREN LAWRENCE CLASSIFICATION : 1
   FOLLOW UP

1. AT 0 MONTHS

   VAS SCORE : 6.4
   WOMAC SCORE : 66

2. AT 3 MONTHS

   VAS SCORE : 4.7
   WOMAC SCORE :41

3. AT 6 MONTHS

   VAS SCORE : 1.9
   WOMAC SCORE : 19

INTRA-ARTICULAR HYALURONIC ACID INJECTION

CASE NO. : 1

NAME : LAKSHMIBAI

AGE/SEX : 66/F

O P NO : 267573

DATE OF INJECTION : 03/02/2024

OCCUPATION : MAID

RESIDENCE : INDI, BIJAPUR

Presenting complaints:

History of pain:
C/O PAIN OVER LEFT KNEE SINCE 1.5 YEARS NO HISTORY OF TRAUMA

d. Duration of pain :
1.5 YEARS

e. Nature of pain :

GRADUALLY PROGRESSIVE EXAGERATED ON FLEXION AND WEIGHT BEARING

c. History of past medical disease

- Diabetes mellitus :NIL
- Hypertension /IHD: NIL

d. Personal and family history
NOTHING SIGNIFICANT

Examination

General physical examination

6. Built and nourishment
   BMI : 26.8

7. Signs
   Injection site redness , fever , chills :ABSENT

8. Vital parameters:

   Pulse : 82 BPM

   BP: 140/90 mm hg

9. VAS SCORE : 6.4

10. WOMAC SCORE : 60

Systemic Examination
CVS : S1 AND S2 HEARD NO MURMUR

RS : B/L NVBS PRESENT

P/A : SOFT NON TENDER

CNS : ALERT CONSCIOUS ORIENTED

Local Examination

(a) Inspection
GENERALISED SWELLING PRESENT

(b) Palpation

- Temperature : NO LOCAL RISE OF TEMPERATURE
- Tenderness : PRESENT OVER MEDIAL JOINT LINE
- Crepitus on range of movements : PRESENT

TREATMENT

INTRA ARTICULAR INJECTION GIVEN :

DOSE 1 ON 03/02/2024
DOSE 2 ON 05/03/2024
DOSE 3 ON 08/04/2024

INVESTIGATIONS

2. X-RAY KNEE STANDING AP LATERAL
Osteophytes : PRESENT
Decrease in joint space : REDUCED
KELLGREN LAWRENCE CLASSIFICATION: GRADE 2

FOLLOW UP

4. AT 0 MONTHS

VAS SCORE : 6.4
WOMAC SCORE : 60

5. AT 3 MONTHS

VAS SCORE : 3.5
WOMAC SCORE : 28

6. AT 6 MONTHS

VAS SCORE : 3.2
WOMAC SCORE : 26

IMAGES

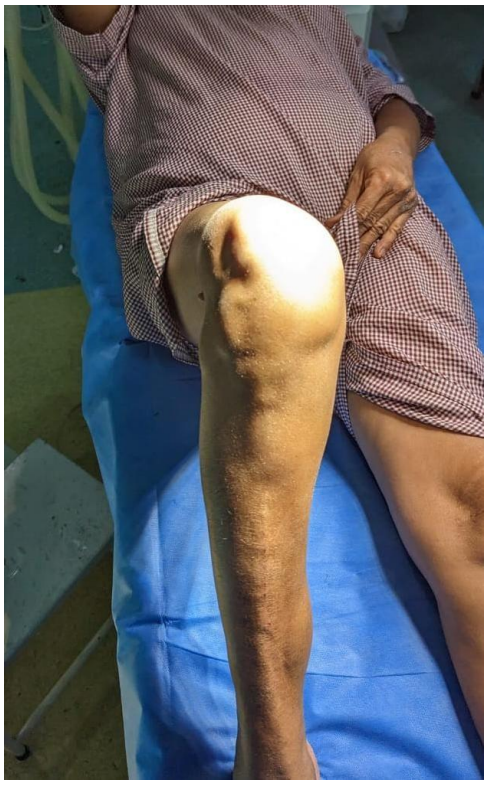


Fig 9: positioning for knee intra articular injection

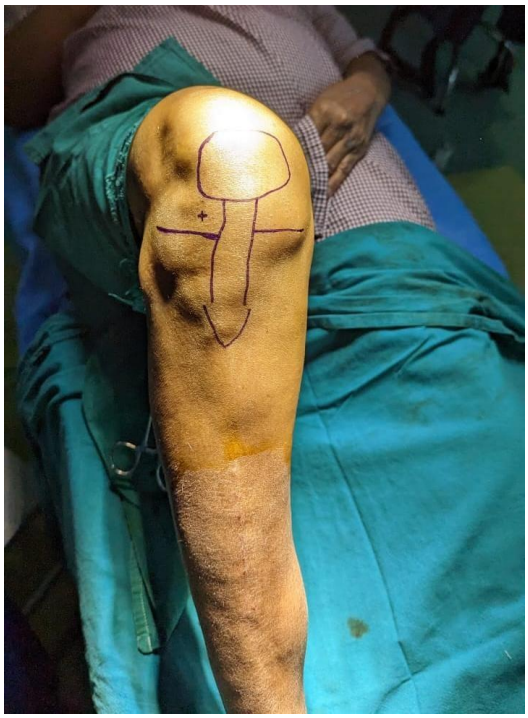


Fig10: landmarks for knee intra articular injection

PRP INJECTION

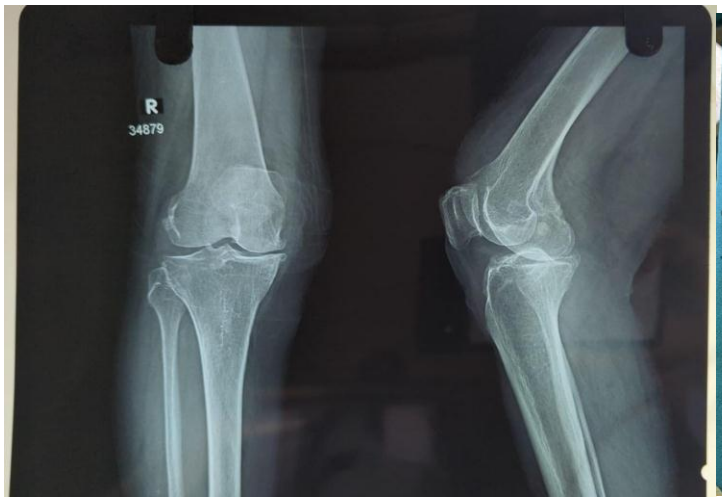


Fig 11: x ray of PRP patient case study

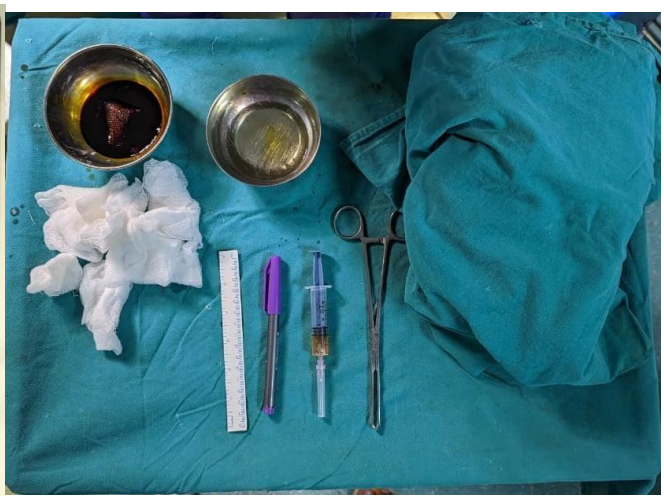


Fig 12 : trolley for knee intra articular injection with PRP

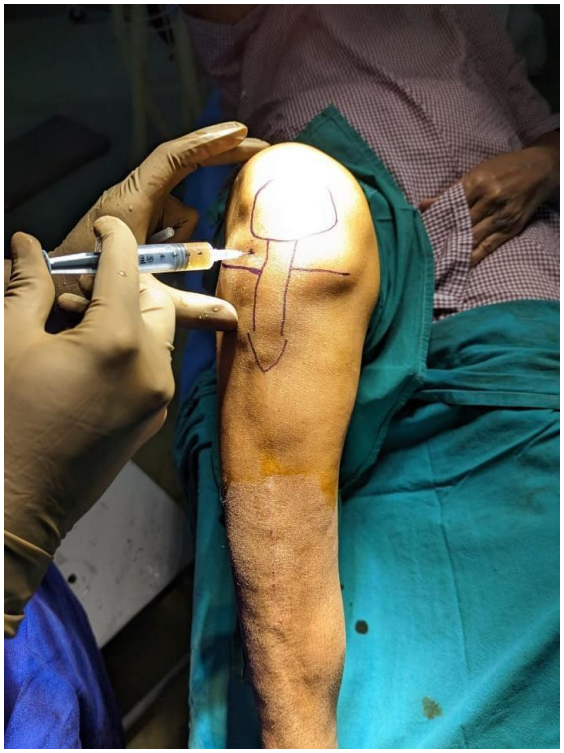


Fig 13 :intra articular PRP injection being given

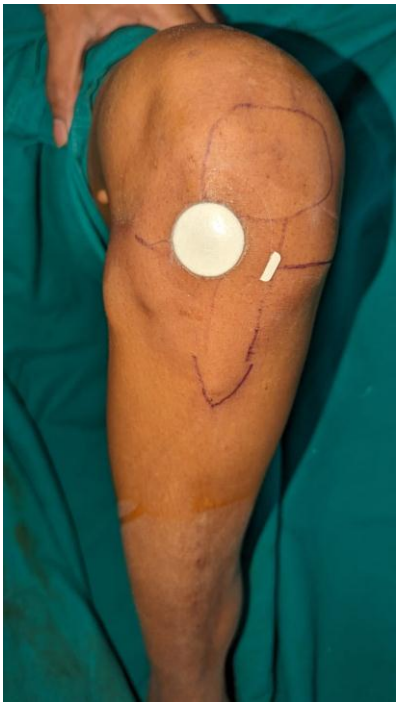


Fig 14 :post intra articular injection

HYALURONIC ACID INJECTION

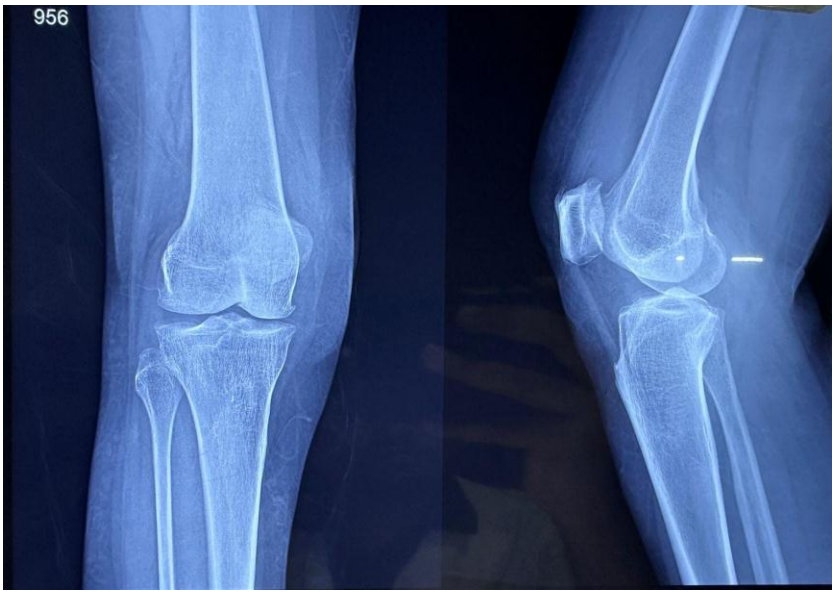


Fig 15: x ray of hyaluronic acid case study

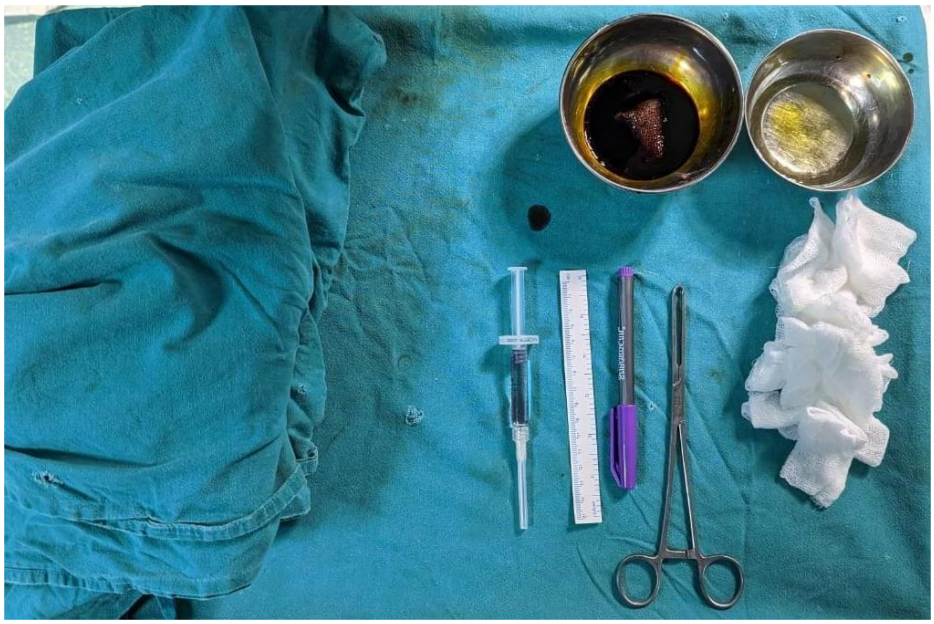


Fig 16 : trolley for knee intra articular hyaluronic acid injection

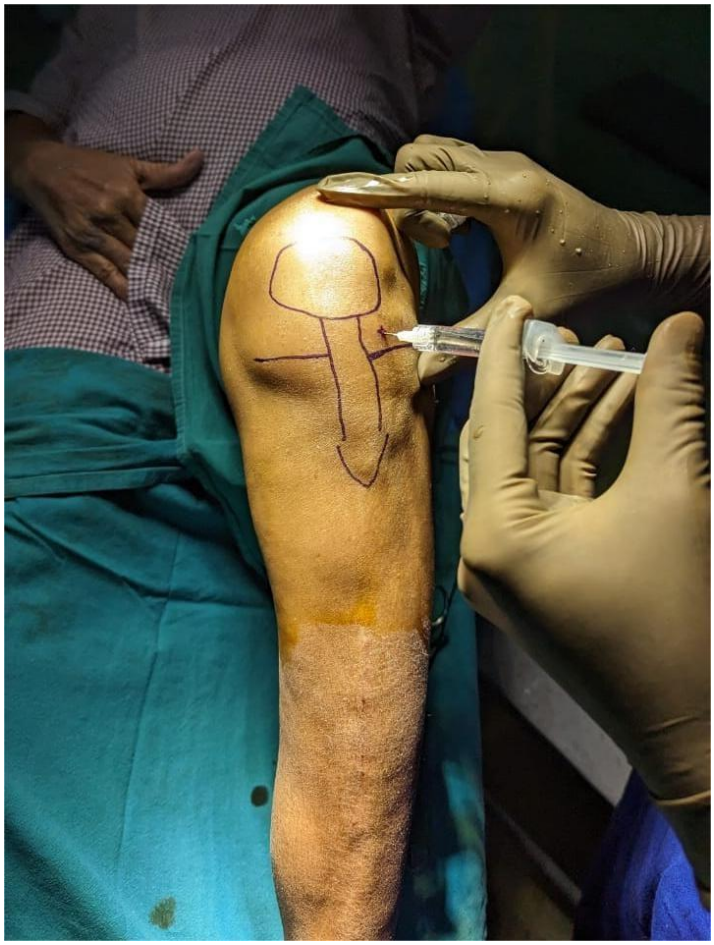


Fig 17: positioning and intra articular hyaluronic acid injection

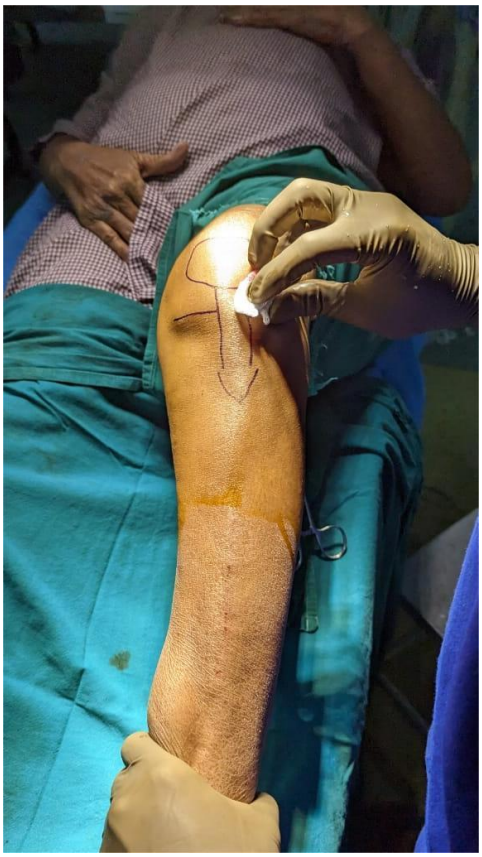


Fig 18: post hyaluronic aid injection

DISCUSSION

Osteoarthritis (OA) of the knee is a prevalent degenerative joint disease characterized by progressive cartilage deterioration, subchondral bone remodeling, osteophyte formation, and synovial inflammation, resulting in pain, stiffness, and impaired joint function. The global prevalence of knee OA has been increasing steadily, affecting approximately 16% of adults aged 45 years and older, with significant socioeconomic implications due to healthcare costs and reduced work productivity.[68] Traditional treatment approaches include analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), physical therapy, and ultimately, surgical interventions for advanced cases. However, these conventional methods primarily address symptomatic relief rather than targeting the underlying pathophysiological processes of OA. In recent years, intra-articular injections of biologic agents, specifically hyaluronic acid (HA) and platelet-rich plasma (PRP), have gained significant attention as potentially disease-modifying interventions for knee OA.[69] The present study was undertaken to compare the efficacy and safety profiles of intra-articular PRP versus HA in patients with mild to moderate knee OA.

Demographic and Baseline Characteristics

Our study included 70 patients with knee OA, equally distributed between the HA and PRP groups (35 patients each). The demographic characteristics of both groups were comparable in terms of age distribution, with the majority of patients (34.3% in both groups) in the 41-50 years age bracket. There was a slightly higher proportion of male patients in the PRP group (74.3%) compared to the HA group (54.3%), though this difference did not reach statistical significance ($p=0.08$). The BMI distribution was remarkably similar between groups, with approximately half of the patients in both groups being overweight (BMI 25-29.9) and about one-third being obese (BMI >30), reflecting the recognized association between elevated BMI and knee OA.[70]

These demographic findings are comparable to those reported by Raeissadat et al.[71] who conducted a similar comparative study between PRP and HA, with a mean participant age of 56.85 ± 9.13 years in the

PRP group and 61.10 ± 7.57 years in the HA group. Similarly, Montañez-Heredia et al.[72] reported a mean age of 66.3 ± 8.2 years for their study population comparing PRP and HA, with a slightly higher proportion of female participants (67% overall), contrasting with our predominance of male patients, particularly in the PRP group.

The Kellgren-Lawrence (KL) radiographic grading revealed that 60% of patients in the PRP group had grade 1 OA, compared to 42.9% in the HA group, while 40% in the PRP group had grade 2 OA versus 57.1% in the HA group. Although this suggests a slightly higher proportion of grade 2 OA in the HA group, the difference was not statistically significant (p=0.15). This distribution is important when interpreting clinical outcomes, as previous studies have suggested that response to intra-articular injections may vary based on OA severity.[73]

The distribution of affected knees (left, right, or bilateral) was also comparable between groups (p=0.55), with unilateral involvement being predominant in both groups. Notably, the HA group had a slightly higher proportion of bilateral knee involvement (17.1%) compared to the PRP group (8.6%), which could potentially influence patient-reported outcomes.

Clinical Outcomes

Pain Assessment (VAS)

Pain reduction, as measured by the Visual Analog Scale (VAS), demonstrated an interesting temporal pattern in our study. At baseline, both groups had comparable mean VAS scores (6.5±0.81 for HA and 6.5±0.8 for PRP; p=0.84), indicating moderate to severe pain levels. At the 3-month follow-up, the HA group showed significantly better pain reduction (3.12±0.48) compared to the PRP group (4.65±0.68; p<0.001). However, this pattern reversed dramatically at the 6-month follow-up, with the PRP group demonstrating superior pain relief (2.08±0.45) compared to the HA group (3.14±0.51; p<0.001).

This temporal evolution of comparative efficacy between PRP and HA aligns with findings from several previous studies. Görmeli et al.[74] conducted a randomized controlled trial comparing single and triple PRP injections with HA in 162 patients with knee OA and found that while both interventions provided

significant pain relief, PRP showed superior and more sustained improvements, particularly for early-stage OA. Similarly, Cole et al.[75] in their randomized trial of 111 patients with knee OA reported that while both PRP and HA treatments resulted in significant clinical improvements, the PRP group maintained significantly better outcomes at 24 and 52 weeks.

The initial superiority of HA at 3 months followed by better outcomes with PRP at 6 months in our study suggests different mechanisms of action and durability for these two interventions. HA primarily provides viscosupplementation and acts as a lubricant, potentially offering more immediate symptomatic relief. In contrast, PRP contains numerous growth factors and bioactive proteins that may stimulate cartilage matrix synthesis, modulate inflammation, and promote tissue regeneration, potentially explaining its superior long-term efficacy.[76] This mechanism aligns with the systematic review and meta-analysis by Tang JZ et al.[77], which concluded that PRP injections provided better pain relief than HA at 6 and 12 months post-injection.

Functional Assessment (WOMAC)

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores in our study followed a pattern similar to the VAS scores. Baseline WOMAC scores were comparable between groups (67.4±6.4 for HA and 68.2±6.4 for PRP; $p=0.55$). At 3 months, the HA group demonstrated significantly better functional improvement (31.7±4.3) compared to the PRP group (47.2±5.4; $p<0.001$). However, by 6 months, the PRP group showed markedly superior functional outcomes (22.11±3.2) compared to the HA group (32.4±4.6; $p<0.001$).

This temporal evolution of functional outcomes mirrors the findings of several previous investigations. Lana et al.[78] conducted a randomized clinical trial comparing HA, PRP, and combined therapy in 105 patients with knee OA and reported that while all interventions improved WOMAC scores, PRP and combined therapy resulted in better maintenance of functional improvements at 1-year follow-up. Di Martino et al.[79] in their randomized controlled trial with 192 patients reported that both PRP and HA significantly improved WOMAC scores, with PRP showing a trend toward better results, particularly in

patients with early OA.

The reversal pattern observed in our study, with HA showing better early outcomes and PRP demonstrating superior longer-term results, may reflect the different biological mechanisms of these interventions. HA potentially provides immediate improvement through enhanced joint lubrication and anti-inflammatory effects, while PRP's regenerative and anti-inflammatory properties may take longer to manifest but provide more sustainable benefits.[80] This temporal pattern is particularly important in clinical decision-making, as the choice between PRP and HA might depend on whether the primary goal is short-term or longer-term symptom management.

Complications and Safety Profile

The safety profiles of PRP and HA in our study revealed some notable differences. The PRP group demonstrated a superior safety profile with 91.4% of patients experiencing no complications, compared to 74.3% in the HA group. Specifically, the HA group reported complications including infection (5.7%), residual pain (8.6%), and synovitis (11.4%), while the PRP group only reported residual pain (8.6%). Although the overall difference in complication rates did not reach statistical significance (p=0.09), the absence of infection and synovitis in the PRP group is clinically relevant.

The higher incidence of synovitis in the HA group (11.4%) compared to none in the PRP group is particularly noteworthy and consistent with previous literature. Patel et al.[81] reported transient pain and swelling after HA injections, attributing this to a possible inflammatory response to exogenous hyaluronic acid. Similarly, Sundman et al.[82] demonstrated in an in vitro study that PRP had anti-inflammatory effects through suppression of inflammatory mediators, potentially explaining the lower incidence of post-injection synovitis.

The absence of infections in the PRP group despite its more complex preparation process is reassuring and consistent with previous safety assessments. Riboh et al.[83] in their meta-analysis of randomized controlled trials found no significant increase in adverse events with PRP compared to placebo or HA, while Filardo et al.[84] reported only minor and transient adverse events associated with PRP injections, primarily

post-injection pain.

The safety advantage of PRP may be attributed to its autologous nature, reducing the risk of immune-mediated reactions, and to the presence of antimicrobial peptides like platelet factor 4, RANTES, and connective tissue-activating peptide 3, which have been shown to have bactericidal and bacteriostatic properties.[85] This safety profile, combined with its superior long-term efficacy, supports the use of PRP as a favorable option for knee OA management.

Interpretation in Context of Disease Severity

The distribution of OA severity in our study population, as measured by the Kellgren-Lawrence (KL) grading system, showed a slightly higher proportion of grade 1 (mild) OA in the PRP group (60% vs 42.9% in HA group) and grade 2 (moderate) OA in the HA group (57.1% vs 40% in PRP group). This difference, although not statistically significant ($p=0.15$), could potentially influence treatment outcomes, as previous research has suggested differential responses to biologics based on OA severity.

Campbell et al.[86] in their systematic review found that patients with early to moderate OA (KL grade 1-2) typically respond better to PRP than those with advanced disease. Similarly, Kon et al.[87] reported that the efficacy of PRP decreased with increasing severity of degenerative changes. Our finding of superior long-term outcomes with PRP despite the balanced distribution of OA severity suggests that PRP's benefits may be applicable across the spectrum of mild to moderate knee OA.

The efficacy of HA has also been shown to vary with OA severity. Bowman et al.[88] reported that HA provided significant pain relief in mild to moderate OA but showed limited efficacy in severe cases. The initial superiority of HA at 3 months in our study, particularly for functional outcomes, may suggest that HA provides valuable short-term benefits irrespective of OA severity within the mild to moderate range.

Pathophysiological Considerations

The differential temporal efficacy pattern observed in our study may be explained by the distinct mechanisms of action of PRP and HA in the context of OA pathophysiology. Knee OA involves cartilage degradation, subchondral bone alterations, synovial inflammation, and impaired joint homeostasis. HA, as a

principal component of synovial fluid, primarily functions through mechanical effects (shock absorption, lubrication) and biological effects (anti-inflammatory, chondroprotective) that may provide immediate symptomatic relief.[89]

In contrast, PRP contains a concentrated cocktail of growth factors including platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), insulin-like growth factor-1 (IGF-1), vascular endothelial growth factor (VEGF), and fibroblast growth factor (FGF). These factors have been shown to stimulate chondrocyte proliferation, enhance cartilage matrix synthesis, reduce matrix degradation, and modulate inflammation through multiple signaling pathways.[76] The activation of these regenerative pathways may take longer to manifest clinically, potentially explaining the superior long-term outcomes observed with PRP in our study.

Importantly, PRP's anti-inflammatory effects may extend beyond symptomatic relief to potentially address underlying pathophysiological processes. Osterman et al.[90] demonstrated that PRP reduces expression of inflammatory cytokines like TNF-α, IL-1β, and catabolic enzymes such as matrix metalloproteinases (MMPs) in synovial fibroblasts. This anti-inflammatory action may explain the lower incidence of synovitis in our PRP group compared to the HA group.

Clinical Implications and Future Directions

The findings of our study have several important clinical implications. First, the temporal evolution of efficacy suggests that the choice between PRP and HA should consider the desired duration of effect and patient-specific factors. For patients requiring immediate symptom relief, HA may be preferable, while PRP may be more appropriate for those seeking longer-term benefits.

Second, the superior safety profile of PRP, particularly the absence of synovitis and infection, supports its use in clinical practice, especially for patients with a history of adverse reactions to previous intra-articular therapies or those at higher risk of infection.

Third, although our study demonstrated superior long-term outcomes with PRP, the optimal preparation protocol, injection frequency, and patient selection criteria remain to be standardized. The heterogeneity in

PRP preparation methods, including variations in platelet concentration, activation status, and leukocyte content, may influence clinical outcomes and should be considered in future investigations.[91]

Looking ahead, several aspects warrant further exploration. Larger multicenter trials with longer follow-up periods are needed to confirm the durability of PRP benefits beyond 6 months. Studies investigating the combination of PRP with other therapeutic modalities, such as HA, corticosteroids, or physical therapy, could potentially optimize treatment outcomes. Additionally, advanced imaging and biochemical marker studies may help elucidate the structural and molecular effects of PRP on cartilage and synovium, providing insights into its disease-modifying potential.

Strengths and Limitations

Our study has several strengths, including the prospective design, equal distribution of patients between groups, comprehensive assessment of pain and function using validated tools (VAS and WOMAC), and detailed documentation of complications. The inclusion of patients with mild to moderate OA (KL grade 1-2) allows our findings to be applicable to the population most likely to benefit from intra-articular therapies.

However, certain limitations should be acknowledged. The follow-up period of 6 months may not be sufficient to assess the long-term durability of treatment effects. The absence of a placebo control group limits our ability to account for the natural history of the disease and placebo effect. Additionally, the lack of advanced imaging or biochemical marker assessments prevents direct evaluation of structural or molecular changes in cartilage and synovium. The single-center nature of our study and the relatively small sample size may limit generalizability, although our findings are consistent with larger multicenter investigations.

Conclusion

In conclusion, our comparative study of intra-articular PRP versus HA in patients with mild to moderate knee OA demonstrates a distinct temporal efficacy pattern, with HA providing superior short-term improvements in pain and function at 3 months, while PRP shows significantly better outcomes at 6 months. PRP also demonstrated a more favorable safety profile, with no cases of infection or synovitis compared to HA. These findings suggest that PRP may be the preferred option for long-term management of knee OA,

particularly in patients seeking sustained symptom relief and functional improvement. Further research with larger sample sizes, longer follow-up periods, and assessment of structural changes is warranted to fully elucidate the disease-modifying potential of these biological interventions.

CONCLUSION

Osteoarthritis of the knee is a debilitating condition that significantly impacts quality of life and poses substantial socioeconomic burden. This study aimed to compare the efficacy and safety of two commonly used intra-articular interventions: platelet-rich plasma (PRP) and hyaluronic acid (HA) in the management of mild to moderate knee OA. Based on our findings, we can draw several important conclusions.

Our study demonstrated a distinct temporal pattern in the comparative efficacy of PRP and HA. While HA provided superior pain relief and functional improvement at 3 months post-injection, PRP demonstrated significantly better outcomes at 6 months. This temporal evolution suggests different mechanisms of action and durability for these two biological interventions. The initial superiority of HA likely reflects its immediate viscosupplementation and lubricating properties, whereas the long-term benefits of PRP may be attributed to its regenerative potential and modulation of inflammatory pathways.

From a safety perspective, PRP exhibited a more favorable profile, with no cases of infection or synovitis compared to the HA group. This advantage can be attributed to the autologous nature of PRP, which minimizes immune-mediated reactions, and to the presence of antimicrobial peptides that provide inherent protection against infections. The absence of synovitis in the PRP group is particularly noteworthy and clinically relevant for patients with inflammatory phenotypes of knee OA.

The correlation between patient demographics, disease characteristics, and treatment outcomes in our study suggests that both interventions are effective across the spectrum of mild to moderate knee OA (Kellgren-Lawrence grades 1-2). However, the sustained benefits observed with PRP support its use as a preferential option for longer-term management, particularly in patients seeking durable symptom relief and functional improvement.

In conclusion, while both PRP and HA are effective interventions for knee OA, their distinct temporal efficacy patterns and safety profiles should guide clinical decision-making. PRP emerges as the preferred option for long-term management, especially in patients who can tolerate the initial lag in maximal

therapeutic response. Future research should focus on optimizing preparation protocols, elucidating mechanisms of action, and investigating potential synergistic effects with other therapeutic modalities to enhance outcomes in knee OA management.

SUMMARY

INTRODUCTION

Osteoarthritis (OA) of the knee is a prevalent degenerative joint disease characterized by progressive cartilage deterioration, pain, and functional limitation. Intra-articular injections of biologic agents have emerged as potential disease-modifying interventions for knee OA. This study aimed to compare the efficacy and safety of intra-articular platelet-rich plasma (PRP) versus hyaluronic acid (HA) in the treatment of mild to moderate knee OA

AIMS AND OBJECTIVES

Objectives:

1. To research the use of platelet-rich plasma and intra-articular hyaluronic acid in the treatment of osteoarthritis in the knee.
2. To assess PRP's effectiveness and safety in treating mild to moderately symptomatic knee osteoarthritis compared to hyaluronic acid.
3. Research side effects of intra-articular injections used to treat osteoarthritis

MATERIAL AND METHODS

In this prospective comparative study, 70 patients with Kellgren-Lawrence grade 1-2 knee OA were randomly allocated to receive either PRP (n=35) or HA (n=35) intra-articular injections. Patients were evaluated at baseline, 3 months, and 6 months post-injection using the Visual Analog Scale (VAS) for pain and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for functional assessment. Complications and adverse events were recorded throughout the follow-up period.

RESULTS

The key findings of our study can be summarized as follows:

1. Demographic and baseline characteristics: Both groups were comparable in terms of age distribution (predominantly 41-50 years), BMI (mostly overweight and obese categories), and radiographic severity. The PRP group had a slightly higher proportion of male patients (74.3% vs 54.3% in HA group) and grade 1 OA (60% vs 42.9% in HA group), though these differences did not reach statistical significance.
2. Pain outcomes (VAS scores): At baseline, both groups had comparable pain levels (6.5±0.81 for HA and 6.5±0.8 for PRP). At 3 months, the HA group showed significantly better pain reduction (3.12±0.48) compared to the PRP group (4.65±0.68; $p<0.001$). However, at 6 months, this pattern reversed, with the PRP group demonstrating superior pain relief (2.08±0.45) compared to the HA group (3.14±0.51; $p<0.001$).
3. Functional outcomes (WOMAC scores): Baseline WOMAC scores were comparable between groups (67.4±6.4 for HA and 68.2±6.4 for PRP). At 3 months, the HA group demonstrated significantly better functional improvement (31.7±4.3) compared to the PRP group (47.2±5.4; $p<0.001$). By 6 months, the PRP group showed markedly superior functional outcomes (22.11±3.2) compared to the HA group (32.4±4.6; $p<0.001$).
4. Complications: The PRP group demonstrated a superior safety profile with 91.4% of patients experiencing no complications, compared to 74.3% in the HA group. The HA group reported complications including infection (5.7%), residual pain (8.6%), and synovitis (11.4%), while the PRP group only reported residual pain (8.6%).

These results demonstrate a temporal pattern in the comparative efficacy of PRP and HA, with HA providing better short-term outcomes at 3 months and PRP demonstrating superior long-term benefits at 6 months, along with a more favorable safety profile. These findings suggest that PRP may be the preferred option for long-term management of knee OA, particularly in patients seeking sustained symptom relief and functional improvement.

CONCLUSION:

Intra-articular PRP and HA demonstrate a distinct temporal efficacy pattern in knee OA management, with HA providing superior short-term benefits at 3 months and PRP showing significantly better long-term outcomes at 6 months. PRP also exhibited a more favorable safety profile. These findings suggest that PRP may be the preferred option for long-term management of mild to moderate knee OA, particularly in patients seeking sustained symptom relief and functional improvement.

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ANNEXURE

PROFORMA

CASE NO. :

FOLLOW UP NO :

NAME :

AGE/SEX :

I P NO :

DATE OF ADMISSION :

DATE OF SURGERY:

DATE OF DISCHARGE :

OCCUPATION :

RESIDENCE :

Presenting complaints:

History of pain:

f. Duration of pain

g. Nature of pain

c. History of past medical disease

- Diabetes mellitus
- Hypertension /IHD

d. Personal and family history

Examination

General physical examination

11. Built and nourishment
    b. BMI

12. Signs
    Injection site redness , fever , chills

13. Vital
    parameters:

    Pulse :

    BP :

14. VAS SCORE

15. WOMAC SCORE

Systemic Examination

CVS

RS

P/A

CNS

Local Examination

(a) Inspection
Redness ,swelling , discharging sinus

(b) Palpation

- Temperature
- Tenderness
- Crepitus on range of movements

TREATMENT

INTRA ARTICULAR INJECTION GIVEN : PRP/HYALURONIC ACID

DOSE 1 AT MONTH 1
DOSE 2 AT MONTH 2
DOSE 3 AT MONTH 3

INVESTIGATIONS

3. X-RAY KNEE STANDING AP LATERAL
   Osteophytes
   Decrease in joint space

FOLLOW UP

7. AT 0 MONTHS

   VAS SCORE
   WOMAC SCORE

8. AT 3 MONTHS

   VAS SCORE
   WOMAC SCORE

9. AT 6 MONTHS

   VAS SCORE
   WOMAC SCORE

B.L.D.E. (DEEMED TO BE UNIVERSITY) SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTER, VIJAYAPURA-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

I, the undersigned,_____, S/O D/O W/O _____, aged __years, ordinarily resident of _____ do hereby state/declare that Dr. Manish M of Shri. B. M. Patil Medical College Hospital and Research Centre has examined me thoroughly on _____ at _____(place) and it has been explained to me in my own language that I am suffering from _____ disease (condition) and this disease/condition mimic following diseases. Further Dr. Manish M informed me that he/she is conducting dissertation/research titled "COMPARITIVE STUDY BETWEEN INTRA-ARTICULAR PLATELET RICH PLASMA AND HYALURONIC ACID IN TREATMENT OF OSTEOARTHRITIS OF KNEE" under the guidance of Dr. Dayanand B B requesting my participation in the study. Apart from routine treatment procedure, the pre-injection, , post-injection and follow-up observations will be utilized for the study as reference data.

Doctor has also informed me that during conduct of this procedure, adverse results may be encountered. Most of them are treatable but are not anticipated hence there is chance of aggravation of my condition and in rare circumstances it may prove fatal in spite of anticipated diagnosis and best treatment made

available. Further Doctor has informed me that my participation in this study help in evaluation of the results of the study which is useful reference to treatment of other similar cases in near future, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not assessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on information given by me, I can ask any clarification during the course of treatment / study related to diagnosis, procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Shri/Smt _____under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of patient:

Signature of doctor:

Witness: 1.

2.

Date:

Place :

sl.no	name	age	gender	BMI	Kellgren lawrence gra	affected kn	group	VAS basel	VAS 3 mn	VAS 6 mn	WOMAC baseli	WOMAC 3 mn	WOMAC 6 mn	complicatio
	PRP													
1	Girimalappa	55	Male	26.2	1	Right	PRP	6.4	4.7	1.9	66	41	19	Absent
2	anwar	56	Male	22.3	2	Left	PRP	6.6	4.4	2.2	72	50	24	Absent
3	mallappa	59	Male	27.2	2	Right	PRP	5.4	4.2	1.5	61	39	18	Absent
4	prakash	42	Male	30.8	2	Right	PRP	7.8	5.5	2.5	61	38	22	Absent
5	pundalik	41	Male	23.8	1	Left	PRP	6.9	4.8	2	74	49	20	Absent
6	sudeep k	71	Male	26.4	1	Left	PRP	6.4	4.5	2	66	48	21	Absent
7	yallawwa	71	Female	29.9	1	Left	PRP	8	5.8	2.6	72	55	25	Absent
8	ashok	59	Male	26.1	1	Right	PRP	5.7	4	1.7	62	40	18	Residual pain
9	kavya kumar	66	Female	29	1	Left	PRP	7.4	5.1	2.2	74	54	22	Absent
10	mallikarjun gouda	52	Male	32.2	2	Right	PRP	5	3.4	1.3	64	45	19	Absent
11	parvati	65	Female	24	2	Right	PRP	7.7	6	2.9	57	37	19	Absent
12	s m hiremat	46	Male	27	2	Left	PRP	5.8	4.3	1.5	78	51	29	Absent
13	mallikarjun patil	50	Male	28.4	1	Right	PRP	6	4.4	1.9	74	51	26	Absent
14	neelamma	43	Female	32.4	2	Left	PRP	6.8	4.3	2.6	68	52	21	Absent
15	gurusidappa	40	Male	28.2	1	Right	PRP	5.8	3.5	1.7	63	45	25	Absent
16	shivanand	61	Male	28.6	1	Bilateral	PRP	6.1	3.8	2.4	69	44	21	Residual pain
17	sushilbai	43	Female	34.8	2	Left	PRP	5.5	3.9	1.4	65	48	19	Absent
18	neela gouda	59	Female	33.7	1	Right	PRP	7.5	5.5	2.3	60	44	20	Absent
19	paru chawan	65	Male	27.8	1	Left	PRP	5.9	4.1	1.7	71	46	25	Absent
20	kashibai	49	Female	24	2	Bilateral	PRP	7.5	5	2.5	67	46	23	Absent
21	anil biradar	69	Male	25.8	1	Left	PRP	5.6	4.1	1.5	68	49	21	Absent
22	kollappa	65	Male	27.2	2	Left	PRP	5.7	4	2	74	55	27	Absent
23	irappa	50	Male	30.4	2	Left	PRP	6.8	5	2	59	44	21	Absent
24	sangappa	64	Male	30.8	1	Right	PRP	6	4.5	2.4	61	39	16	Absent
25	mahadevappa	51	Male	33.8	2	Left	PRP	6.4	4.3	2.1	76	49	24	Residual pain
26	rahul p	68	Male	26.7	1	Bilateral	PRP	5.9	4.1	2.3	70	45	23	Absent
27	shreedevi	75	Female	31.5	2	Left	PRP	7.6	5.7	2.8	74	51	22	Absent
28	tukaram	61	Male	32.2	1	Right	PRP	7.3	4.8	2	62	44	18	Absent
29	chandrashekar	50	Male	33.9	1	Left	PRP	6.3	4.7	1.6	78	51	21	Absent
30	shrinath	67	Male	33.6	1	Left	PRP	7.3	5.8	2.9	57	44	19	Absent
31	priya	40	Female	22.1	1	Right	PRP	6.5	3.9	2	75	55	27	Absent
32	prakash	53	Male	25.4	2	Right	PRP	8	5.6	3	80	59	29	Absent
33	niranjan	45	Male	29.3	1	Right	PRP	6.7	5	1.7	67	44	23	Absent
34	govind	68	Male	22.8	1	Right	PRP	6.3	5	2.2	75	54	22	Absent
35	pavan	56	Male	27	1	Left	PRP	6.7	5.1	1.8	70	49	25	Absent
	HYALURONIC ACID													
36	gauravva	42	Female	27.9	1	Bilateral	HA	5.6	2.3	2.6	65	28	26	Synovitis
37	shantanu	52	Male	27.9	2	Left	HA	6	2.5	2.7	62	26	30	Absent
38	laxmi bai	66	Female	26.8	2	Left	HA	6.4	3.2	3.5	60	28	26	Absent
39	danamma	55	Female	27.7	2	Left	HA	7.1	3.7	3.5	75	35	36	Synovitis
40	sumanth	57	Male	30.2	2	Bilateral	HA	6	2.8	2.7	70	34	33	Absent
41	jakappa	65	Male	34.4	1	Left	HA	5.4	2.3	2.2	57	25	25	Synovitis
42	sanjay	63	Male	26.7	1	Right	HA	6.3	3.2	3.2	66	32	33	Absent
43	basappa	66	Male	26.2	2	Right	HA	6.7	2.9	2.8	65	32	30	Absent
44	sharanu	64	Male	28.1	1	Bilateral	HA	7.7	3.2	4	65	29	31	Residual pain
45	sharada	47	Female	29.7	2	Left	HA	7.3	3.3	3.2	72	36	34	Absent
46	sidawwa	54	Female	22.5	2	Right	HA	6.5	2.7	2.7	71	34	38	Absent
47	jagadesh	45	Male	31.8	2	Right	HA	6.1	3.3	3.1	68	34	31	Residual pain
48	husam sab	45	Male	26.7	1	Right	HA	6.5	2.9	3.5	60	26	25	Absent
49	ashok	47	Male	28.1	2	Right	HA	6.2	3	3.1	64	27	27	Absent
50	shubhavati	44	Female	23.3	2	Left	HA	7.6	3.7	3.6	70	35	36	Absent
51	zayeeda p	49	Female	24.6	1	Bilateral	HA	7.9	3.4	3.9	78	40	41	Absent
52	tayamma	40	Female	24.6	1	Right	HA	6.1	2.7	3.2	78	36	40	Absent
53	niranjan	71	Male	26.3	1	Left	HA	6.6	3	3.4	58	30	30	Absent
54	nagamma	74	Female	31.5	2	Right	HA	7.3	4	3.8	63	31	33	Absent
55	nandesh	68	Male	26.1	2	Right	HA	5.7	3.1	2.7	59	27	28	Absent
56	mehboob	48	Male	29	1	Bilateral	HA	6	2.7	3	72	33	38	Absent
57	sureka	74	Female	22.1	1	Right	HA	7.3	3.6	3.6	65	29	31	Absent
58	sreeleela	48	Female	34.7	2	Bilateral	HA	5.9	3.1	2.6	76	39	38	Residual pain
59	elizabeth	57	Female	34.9	2	Left	HA	7.2	3.3	3.6	76	34	33	Absent
60	govind	51	Male	34.4	1	Right	HA	7.1	3.5	3.9	60	30	29	Absent
61	mahesh	71	Male	33.6	2	Left	HA	6.3	2.5	2.5	65	31	30	Absent
62	manikanth	40	Male	22.7	2	Left	HA	5.9	2.7	3	76	40	40	Absent
63	parvati	57	Female	34.3	1	Right	HA	6.3	3.1	3	77	34	37	Absent
64	jemarubai	43	Female	30.1	1	Left	HA	5.4	2.7	2.8	79	39	41	Absent
65	jakanna	57	Male	24.7	2	Left	HA	6.1	3.2	2.5	61	26	27	Absent
66	amarappa	72	Male	26.2	1	Right	HA	6.7	2.8	2.9	68	29	33	Absent
67	sai laxmi	65	Female	27.5	2	Left	HA	5.5	3	2.2	62	28	29	Infection
68	sangappa	60	Male	23	2	Left	HA	6.8	3.7	3.4	68	37	34	Absent
69	sanganna	72	Male	35	1	Left	HA	7.9	4.3	3.7	62	28	31	Absent
70	husanbai	64	Female	28.2	2	Left	HA	7.7	4.1	4	65	28	30	Infection