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Original Research Article

Comparative Evaluation of Efficacy of Intra-Articular Injection of Platelet Rich Plasma Versus Hyaluronic Acid in Treatment of Early Osteoarthritis of Knee

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Conflict of interest: Nil

Abstract:

Background: Osteoarthritis of the knee is common and often leads to significant physical disability. While classic conservative therapeutic approaches aim for symptoms like pain and inflammation, procedures like the intraarticular application of hyaluronic acids (HA) or platelet-rich plasma (PRP) gives a less invasive treatment and improves functional quality in patients with initial stages of knee osteoarthritis. This study was conducted to compare the efficacy of intra-articular injection of platelet-rich plasma with hyaluronic acid for the treatment of patients with early osteoarthritis of the knee.

Methodology: This Randomized prospective clinical study was conducted at Dr. Patnam Mahender Reddy Medical College, Chevella in Rangareddy, Telangana between March 2022 to February 2023. A total of 100 patients (50 treated with PRP and 50 with HA) were treated with three weekly intra-articular injections. Clinical examinations were performed before treatment, at 6 weeks, 3rd month, and 6th month post-injection intervals. VAS & WOMAC scores were determined at each examination. All patients are subjected to ultrasound of the involved knee joint and joint space is measured and charted out both pre and post-procedurally. Complications were also recorded.

Results: The mean age of patients in group PRP was 49.92+7.72 and group HA was 54.16+5.36. The mean pre-procedural VAS and WOMAC scores of group PRP were 7.22+0.97 and 74.20+4.85 respectively and group HA were 69.80+4.68 and 6.86+0.81. At the end of 12th month, the mean VAS and WOMAC score improved to 3.06+1.24 and 33.40+7.59 in group PRP and 4.98+0.89 and 56.1+4.769 in group HA respectively. By the end of 12th month follow up, 38 (73.58%) patients reported excellent results, 10 (20.75%) patients reported good results and 2 (5.66%) patients reported poor results. By the end of the 12th month follow-up, 35 (75.43%) patients reported excellent results, 10 (19.29%) patients reported good results and 5 (5.26%) patients reported poor results.

Conclusion: Results indicated that intra-articular PRP group shows better functional outcome and reduction in pain component than HA group in OA knee patients.

Keywords: Platelet Rich Plasma, Visco-Supplements, Hyaluronic Acid.

Introduction

The most prevalent joint disease, osteoarthritis (OA), is characterized by a progressive loss of joint cartilage, changes to the synovial membrane, and a decrease in the viscosity of the synovial fluid.[1] The illness's characteristic manifestation is cartilage degradation. According to radiographic imaging,[2] knee OA affects more than 30% of adults over 50. The prevalence of knee osteoarthritis ranges from 6 to 40%, and it rises with age, according to the findings of various studies.[3] In recent years, risk variables other than age, heredity, obesity, joint injuries, occupational or leisure activities, gender, and race, have made athletes and younger people more vulnerable.[4] In

comparison to men, women are more likely to develop knee osteoarthritis.[5] By 2030, it is predicted that more than six times as many people would need knee arthroplasty due to an increase in life expectancy, placing a considerable financial load on pain management and patient rehabilitation.[6]

Pain and physical restrictions that significantly affect a person's quality of life as well as her or his social and economic activities are the most typical signs of knee osteoarthritis.[3,7] In order to reduce pain and symptoms and halt the advancement of arthritis, medication therapies are now utilized in conjunction with visco supplementation. These include opioids, corticosteroids, glucosamine, chondroitin, and sulphate. Sadly, there are presently no treatments that can stop the growth of OA and repair any already done damage. The effectiveness of analgesics and nonsteroidal anti-inflammatory medications (NSAIDs) is subpar, and there are some safety issues due to their well-known gastrointestinal and cardiorenal side effects [8].

Additionally, an effective treatment for early arthritis is intra-articular injection.[9] Platelet-rich plasma (PRP) and hyaluronic acid (HA) are two treatments that are employed.[10,11] A typical adult knee joint has 2 mL of synovial fluid, which has a mean molecular weight of 5-7 106 kD and 2.5–4 mg/mL of HA. Endogenous HA's concentration and molecular weight decrease in the presence of OA because of aberrant synoviocyte production, dilution of synovial fluid brought on by effusion, and molecular fragmentation. The American College of Rheumatology (ACR) guideline recommended visco supplementation as a treatment option for pain reduction in knee OA in 2000, and the Food and Drug Administration approved it for use in knee therapy in 1997. The goal is to restore the joint's lost viscoelasticity. This technique is routinely used and has shown some promising results,[12] however other studies have shown inconsistent results.[13] According to the findings of clinical research including 306 patients, considerably more patients reacted to intra-articular injections of HA than to a placebo at the 40-month visit (P.004).[14] Miller and Block conducted another meta-analysis in 2013 and found that utilising US-approved HA in knee OA patients is both safe and effective. Recent research supports the use of platelet-rich plasma products as an efficient and secure technique for treating knee OA in its early phases.[15] Transforming growth factor, platelet-derived Growth factor, and insulin-like growth factor 1 are a few growth factors found in platelet-rich plasma products that help maintain an equilibrium between anabolism and catabolism on articular cartilage.[16-19] Others, like basic fibroblast growth factor and vascular endothelial growth factor, play chondroinductive activities

The aim of this study was to know efficacy of intra-articular injection of platelet-rich plasma compared to hyaluronic acid for the treatment of patients with early osteoarthritis of the knee.

Materials and Methods:

From March 2022 to February 2023, patients visiting the outpatient orthopedic department of Dr. Patnam Mahender Reddy Medical College, Chevella in Rangareddy, Telangana State were eligible to participate in this prospective, double-blind RCT if they matched the following criteria: Patients with knee OA (according to American College of Rheumatology criteria) aged 40-70 years, with symptoms lasting more than 3 months and not being relieved by medications, and a confirmatory X-ray diagnosis (Kellgren-Lawrence grade 1-4) within the previous 3 months were included in our study.

Exclusion criteria included a history of diabetes, immunodeficiency, and collagen vascular disorders, a history or presence of malignant disorders, an infection or active wound in the knee area, a recent history of severe knee trauma, autoimmune and platelet disorders, treatment with anticoagulant and antiplatelet medications 10 days before injection, use of NSAIDs 2 days before injection, and a history of knee intraarticular corticosteroid injections in the past.

The Ethics Committee of the Dr. Patnam Mahender Reddy Medical College, Chevella in Rangareddy, Telangana accepted our research. The study includes all participants who signed the written consent form. Then Participants in the study underwent a screening visit (visit 1) that included a medical history, physical examination, laboratory testing (complete blood count with differential (CBC diff), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), knee radiography (standing-Anterior-posterior (AP) and lateral views), and a survey of medications and supplements used. The patients were then allocated into two groups, PRP and HA, at random (using a random number table).

Measures of success A senior resident of the orthopaedic department conducted interviews with all patients to complete the visual analogue scale and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire for assessing patients' function. Visual Analogue Scale for Pain, the visual scale grades the patient's felt pain. The WOMAC questionnaire, which comprises five items for pain, two items for stiffness, and 17 items for assessing functional limitation, is commonly used in arthritis research. Each item is graded on a scale of 0 to 5, with lower scores indicating less discomfort and

greater functional status.

Interventions. Participants were referred to the Dr Patnam Mahender Reddy Medical college, laboratory for the PRP preparation and injection process. The PRP was processed using a technique known as differential centrifugation, which is used to prepare autologous PRP. 20 ml of autologous venous blood is drawn into test tubes containing sodium citrate and centrifuged at 3000 rpm for 15 minutes. The resulting plasma containing platelets is then placed into plain test tubes and subjected to a second centrifugation at 5000 rpm for 15 minutes. The resulting solution in the test tube contains upper two-thirds platelet deficient plasma and lower one-third platelet rich plasma. 20 ml of autologous venous blood yielded 3 - 4 ml of autologous platelet rich plasma solution, and the injection was preceded if approved. There was no injection of a local anaesthetic agent. This was because some literature suggested that anaesthetic drugs could not only be harmful to chondrocytes but could also influence platelet activation by changing the pH of the environment. 20.Some studies have also suggested that interaction with endogenous collagen. 21 is beneficial to platelet activation. We did not use external substances in the activation phase, instead allowing the platelets to come into direct contact with the joint collagen to become active. The injection site's skin was prepared and draped, and the liquid PRP was injected sterilely using a 22G needle through the conventional intra-articular injection method (lateral mid patellar in extended knee position or anteromedial in flexed knee position). After 15-20 minutes of rest, patients were instructed to vigorously flex and extend their knees in order for the PRP to disseminate widely across the joint region before changing to a gel. The second injection was given 28 days (4 weeks) after the first, under the identical settings.

In the second group, HA with the brand name Synvisc was administered. Synvisc-One® (hylan G-F 20) is a high molecular weight elastoviscous fluid combining hylan A and hylan B polymers derived from chicken combs. Hylans are hyaluronan (sodium hyaluronate) derivatives. The hyaluronan in Hylan G-F 20 is chemically cross-linked, making it unique. Hyaluronan is a long-chain polymer composed of repeated Na-glucuronate-N-acetylglucosamine disaccharide units. Under stringent aseptic circumstances, Synvisc-One is administered as a single intra-articular injection.

All patients were instructed to bear weight normally, and pain is managed with ice packs. Patients are evaluated for pain and range of motion using the VAS and WOMAC grading systems on (pre-procedure) day 0 and (post-procedure) at the end of the 6 weeks, third, and twelfth months. The data collected from both groups' participants is statistically analyzed using the Mann-Whitney U test and the p value <0.05 was considered significant.

Results:

The 110 included patients were randomly assigned to PRP (n=57) and HA groups (n = 53). Four patients lost to follow-up (seven from the PRP group and three from the HA group), Eventually, the data of 100 patients (50 in the PRP group and 50 in the HA group) were analyzed.

In Group PRP, Out of 50 cases, 40 (80%) were males and 10 (20%) were females and in Group HA, out of 50 cases, 41 (82%) were males and 9 (18%) were females. The age ranged from age of patients in group PRP is 49.92+7.72 and in group HA is 54.16+5.36 as shown in Table 1.

Table 1: Patient's demography

Variables	Group PRP (n=50)	Group HA (n=50)	P values
SEX male	40	41	0.0833
female	10	9	
AGE (Years) mean+SD	49.92+ 7.72	54.16+5.36	0.1120
Range	35-65	35-65	

The mean pre-procedural VAS and WOMAC scores of group PRP were 7.22+0.97 and 74.20+4.85 respectively and group HA were 69.80+4.68 and 6.86+0.81. At the end of 12th month, the mean VAS and WOMAC score improved to 3.06+1.24 and 33.40+7.59 and group B are 4.98+0.89 and 56.1+4.769 respectively as shown in Table 2

Table 2: Comparison of VAS & WOMAC Scores between the groups

Follow up	Group-PRP	Group-HA	P value
	VAS Score		
Pre injection	7.22+0.97	6.86+0.81	0.122
Post injection 12thmonth	3.06+1.24	4.98+0.89	0.001
	WOMAC Score		
Pre injection	74.20+4.84	69.80+4.68	0.211

Post injection			
6 weeks	62.46+6.60	64.10+5.50	0.072
3 months	47.68+8.15	62.46+5.44	0.003
12 months	33.40+7.59	56.1+4.769	0.002

All patients had an ultrasound of the affected knee joint, and the joint space was measured and registered both before and after the procedure. At the end of 12 months, patients in the PRP group had an average increase in joint space of 0.02 cm on ultrasonography of the knee. At the end of the first month of follow-up, 22 (43.39%) patients reported great outcomes, 18 (35.84%) patients reported good results, and 10 (20.75%) patients reported poor results. By the end of the 12-month follow-up, 38 (73.58%) of the patients reported outstanding outcomes, 10 (20.75%) reported good results, and 2 (5.66%) reported poor results due to noncompliance with the treatment plan The complications reported by group HRA participants were pain in 27 cases (50.94%) and swelling in 19 cases (35.84%).

At the end of 12 months, patients in group HA who underwent homologous platelet lysate injection had an average increase in joint space of 0.05 cm on ultrasonography of the knee. By the end of the first month of follow up, 25 (47.36%) patients reported excellent outcomes, 17 (36.84%) patients reported good results, and 7 (15.78%) patients reported poor results. By the end of the 12-month follow-up, 35 patients (75.43%) reported outstanding results, 10 (19.29%) reported good results, and 5 (5.26%) reported poor results. The complications reported by group HR participants were pain in 19 cases (33.33%).

Discussion:

As a chronic degenerative joint disease, OA in the knee is the second major cause of function loss[22], followed by a significant economic and social burden. [23] The aetiology and pathogenesis of knee osteoarthritis are still unknown, [24] the predominant pathological change is articular cartilage deterioration, with related synovial fluid components also altering[25]. The effusion demolished and diluted hyaluronic acid production, causing the molecular weight and concentration of endogenous HA in the knee articular cavity of OA patients to decrease[26-27]. All of the modifications affected articular cartilage viscoelasticity and its capacity to resist mechanical loads and injury.

Extensive evidence in the literature show that intra-articular administration of HA can restore the viscoelastic qualities of the synovial fluid in the knee joint, resulting in pain alleviation and improved joint mobility. Animal studies have revealed that intra-articular HA has anti-inflammatory, anti-apoptotic, anti-angiogenic, and anti-fibrotic properties[28]. A considerable number of clinical investigations have also shown that HA relieves joint pain and improves joint function. [29-31]

According to some researchers, HA therapy for severe knee osteoarthritis is ineffective. After several administrations, the effectiveness of HA decreases [32-33].Furthermore, HA does not promote cartilage regeneration, particularly in elderly patients [34-35].

According to Kon et al[36], LWHA has a molecular weight of less than 1,000 kDa while HWHA has a molecular weight greater than 1,000 kDa. Kon et al[36], Filardo et al[37], Lana et al[38], and Duymus et al[39] employed HWHA in their research, while Say et al[40] and Montanez-Heredia et al[41] used LWHA.

The amount of injections also varied between studies, with a single injection [38,40] two injections, or numerous injections being used. The period between two injections was also different in studies with several injections. Raeissadat et al[42] utilised a one-month gap in their investigation, while Kon et al[36], Duymus et al[39], and Montanez-Heredia et al[41] used two weeks. Gormeli et al. compared HA to multiple-dose or single-dose PRP[43] in a prospective, randomised experiment. There were no differences between HA and single-dose PRP, while multiple-dose PRP outperformed both.

Intraarticular prp increases the concentration of growth factors at the local pathological site, which causes transcription, translation, cell division, chemotaxis, proliferation, differentiation, neoangiogenesis, neovascularisation, and extracellular matrix production.

Farid Mohammed [44] et al investigated the role of platelet rich plasma in patients with osteoarthritis of the knee in 55 individuals, finding a substantial improvement in pain and function in terms of WOMAC scores from baseline to 3 and 6 weeks, 3 and 6 months post injection. During the injections and follow-up periods, no serious adverse effects were noted.

Filardo et al [37] found that clinical improvement in intra-articular PRP therapy is time dependent, with an average duration of 9 months, and that younger patients with lower levels of joint degeneration receive better and longer lasting effects.

They did not demonstrate superior results in

individuals treated for knee OA by comparing PRP to HA in 2012, however there was a trend towards better results with PRP at 6 and 12 months of follow-up.

Spakova' et al [15], on the other hand, found a statistically significant improvement in the clinical score in the PRP group compared to HA after 3 and 6 months of follow-up.

In 50 patients, Naresh Kumar et al [45] investigated the role of platelet rich plasma injection in arthritic knee. The functional outcome was examined using VAS and WOMAC scores, which revealed a statistically significant result with a p value of 0.001. They concluded that PRP shows a significant improvement in pain and functional status of the knee following a single intra-articular PRP injection after 1, 3, and 6 months.

Forogh B et al [46] employed intra-articular platelet rich plasma for subjective pain reduction one month after intra-articular steroid injections in 41 individuals with advanced osteoarthritis. They determined that one intra-articular PRP injection reduces joint pain more and for a longer period of time, alleviates symptoms, improves daily living activity, and improves short-term quality of life.

With a total of 60 symptomatic patients, Bottegoni et al [47] investigated the safety and efficacy of platelet-rich plasma (PRP) intra-articular injections obtained from blood donors (homologous PRP) on elderly patients with early or moderate knee osteoarthritis (OA) who are not candidates for autologous PRP treatment. All patients were given 5 ml of homologous PRP intraarticular injections every 14 days for a total of three injections, and their functional status was assessed by IKDC, KOOS, and EQ-VAS scores. They found a statistically significant improvement from baseline to the 2-month follow-up, and 90% of patients were satisfied at the 6-month check-up. They concluded that whereas homologous PRP has a high safety profile, it only provides short-term therapeutic benefits in older individuals with knee osteoarthritis.

Aside from the differences in the study intervention, another major aspect that influenced the treatment results was the mechanism of PRP and HA in the change in knee OA. The positive benefits of HA may be due to enhanced lubrication based on viscoelasticity and/or improved intra-articular environment by rebuilding the barrier between the synovial membrane and the articular surface.

Growth factors produced by active platelets have a critical purpose in stimulating chondrocyte proliferation and differentiation, regulating collagenase secretion, and regenerating cartilage. PRP supplies various substances to activate the synovial membrane and surrounding tissues, while HA functions as a lubricant. Lana et al 38 concluded that the combination of HA and PRP may be more beneficial than either alone (the combination of HA and PRP resulted in better outcomes than HA alone at up to 1 year and PRP alone at up to 3 months).

Conclusion:

Based on WOMAC and VAS pain scores, we determined that the PRP injections group outperformed the HA injections group in improving functional outcome in OA of the knee at 6 and 12 months of follow-up. Patients treated with PRP experienced higher pain reduction than those in the HA group.

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