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Comparative study between hyaluronic acid & platelet rich plasma in treatment of knee osteoarthritis

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ABSTRACT

Background: Knee osteoarthritis (OA) is a prevalent degenerative joint condition. This study aims to compare the therapeutic potential of Hyaluronic Acid (HA) and Platelet Rich Plasma (PRP) in its management.

Materials and Methods: A comparative study was conducted with patients receiving either HA or PRP injections. Outcome measures included VAS and WOMAC scores, safety profiles, patient satisfaction, and requirement for repeat injections.

Results: PRP-treated patients exhibited superior improvement in VAS and WOMAC scores by the 12-month mark. Adverse reactions were minimal and comparable between groups. Notably, 92% of PRP recipients expressed a willingness for repeat treatment. PRP-treated patients also showcased prolonged therapeutic benefits, with fewer requiring subsequent injections.

Conclusion: PRP outperforms HA in multiple domains, emphasizing its potential as a more effective treatment for knee OA.

1. Introduction

Osteoarthritis (OA) is the most common form of arthritis, affecting millions worldwide, with the knee being one of the most frequently impacted joints.[1] Over the past decades, OA of the knee has been recognized not only as a degenerative disease but also as an active, dynamic process that involves the entire joint, encompassing cartilage degradation, subchondral bone remodelling, osteophyte formation, synovial inflammation, and changes in periarticular muscles.[2] The pathogenesis of knee OA is multifactorial, encompassing biomechanical, genetic, metabolic, and inflammatory factors.[3] Clinically, this leads to pain, stiffness, reduced joint function, and compromised quality of life.[4]

The current treatment modalities for knee OA are directed toward symptom alleviation rather than disease modification.[5] Among non-surgical treatments, pharmaceutical interventions like acetaminophen, NSAIDs, and opioids are routinely prescribed, but their long-term use is limited due to potential adverse effects.[6] In the quest for more efficacious and safer alternatives, intra-articular therapies have gained significant attention. Of these, hyaluronic acid (HA) and platelet-rich plasma (PRP) have emerged as promising therapeutic agents.[7]

Hyaluronic acid, a chief component of synovial fluid and cartilage, bestows the synovial fluid with its viscoelastic properties.[8] In the context of OA, the molecular weight, concentration, and viscoelasticity of HA present in the synovial fluid diminish, leading to decreased joint lubrication and cushioning.[9] Intra-articular HA injections, known as viscosupplementation, aim to restore the physiological environment of the osteoarthritic joint.[10] Numerous studies have demonstrated the pain-relieving effects and functional improvements following HA therapy, attributing its action to anti-

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inflammatory effects, proteoglycan synthesis stimulation, and chondroprotection.[11]

On the other hand, PRP is an autologous preparation from a patient's own blood, enriched with a higher concentration of platelets.[12] Platelets are reservoirs of growth factors and cytokines that modulate inflammation, tissue repair, and regeneration.[13] When injected into the osteoarthritic knee, PRP releases growth factors that may enhance the recruitment, proliferation, and differentiation of cells involved in tissue regeneration.[14] Furthermore, PRP has shown anti-inflammatory properties by inhibiting pro-inflammatory cytokines, thus potentially slowing the progression of OA.[15]

Both HA and PRP have been studied extensively, with multiple randomized controlled trials (RCTs) and meta-analyses suggesting their efficacy over placebo and even over each other in various settings.[16] However, the comparative efficacy, safety profile, and cost-effectiveness of these treatments remain topics of robust debate among researchers and clinicians.[17] The advent of personalized medicine further necessitates the understanding of individual responses to these treatments and the potential for combining them or using them sequentially for enhanced benefits.[18]

Given the global burden of knee OA, the search for effective treatments that can alter the disease course or provide long-term relief is paramount. This article aims to shed light on the current knowledge surrounding the efficacy and safety of intra-articular HA and PRP injections in knee OA by presenting a comprehensive comparative study. It is hoped that such an exploration can guide clinicians in tailoring their therapeutic decisions and inspire further research in this ever-evolving field.

2. Aim

To conduct a comparative evaluation of the therapeutic effects of intra-articular injections of Hyaluronic Acid (HA) and Platelet Rich Plasma (PRP) in patients with knee osteoarthritis.

3. Objectives

3.1. Clinical assessment

1. To evaluate the reduction in pain intensity after treatment using the Visual Analog Scale (VAS).
2. To assess the improvement in joint function and stiffness using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

3.2. Comparative efficacy

1. To compare the therapeutic effects of HA and PRP in terms of pain relief and functional improvement at various time intervals post-injection (e.g., 1 month, 3 months, 6 months, and 1 year).

3.3. Safety evaluation

1. To monitor and document any adverse events or complications associated with both HA and PRP injections during the study period.

3.4. Patient satisfaction

1. To assess patient satisfaction and overall perceived improvement following both treatments.

4. Materials and Methods

4.1. Study design

This was a prospective, randomized controlled trial conducted at Tezpur Medical College and Hospital to compare the efficacy and safety of intra-articular injections of Hyaluronic Acid (HA) and Platelet Rich Plasma (PRP) in patients with knee osteoarthritis.

4.2. Study setting

The study was carried out at the Department of Orthopaedics, Tezpur Medical College and Hospital.

4.3. Study population

Patients diagnosed with knee osteoarthritis based on clinical and radiological criteria who visited the orthopaedic outpatient department of Tezpur Medical College and Hospital were considered.

4.4. Sample size

A total of 50 patients were enrolled in the study, divided into two equal groups of 25 each:

Group A: Patients receiving intra-articular HA injections

Group B: Patients receiving intra-articular PRP injections

4.5. Inclusion criteria

1. Adults aged 40-70 years.
2. Clinically and radiologically confirmed knee osteoarthritis.
3. Moderate pain on the VAS score.

4.6. Exclusion criteria

1. Patients with rheumatoid arthritis or other inflammatory joint diseases.
2. Previous knee surgery or intra-articular injections in the past 6 months.
3. Known allergic reactions to HA or any components of PRP.

4. Systemic or local infections.
5. Coagulation disorders.

4.7. Intervention

1. Group A: Patients were administered intra-articular HA injections as per the manufacturer's protocol under aseptic conditions.
2. Group B: A total of 30 ml of venous blood was drawn from each patient, processed to obtain PRP, and then administered as an intra-articular injection under aseptic conditions.

Both groups were advised to follow a standard post-injection rehabilitation protocol which included rest, cold compresses, and gradual return to activity.

4.8. PRP preparation

In the preparation of platelet-rich plasma (PRP), all procedures were adhered to under strict aseptic precautions. For the injection of PRP into a single knee, about 8-10 ml of blood was drawn from the antecubital vein. When the requirement was to inject PRP into both knees, approximately 16-18 ml of blood was extracted. This blood was promptly collected in sterile sodium citrate-coated vials.

Without any delay, the blood was centrifuged for two minutes at a rate of 2,500 revolutions in a centrifuge machine housed in the blood bank. Following centrifugation, PRP was carefully separated from the blood, ensuring that all necessary precautions were maintained. A small portion of this separated PRP was reserved for platelet count measurements, while the majority was immediately prepared for knee injection.

For the administration of the PRP injection, the patient was placed in a supine position. The intended injection area was thoroughly cleaned and draped. An 18-22 gauge needle was then inserted into the superolateral aspect of the knee joint, specifically targeting the suprapatellar space. If any joint effusion was present, it was aspirated using a sterile syringe. Following the injection, a sterile band-aid was applied to the injection site, and the knee was flexed and extended multiple times to ensure even distribution of the PRP. After the procedure, patients were permitted to resume their daily activities without restriction.

4.9. Statistical analysis

Data was entered and analysed using SPSS version 25. Descriptive statistics, paired t-tests, and chi-square tests were utilized as appropriate. A p-value < 0.05 was considered statistically significant.

Figure 1: Preparation of platelet-rich plasma (PRP) for Injection.

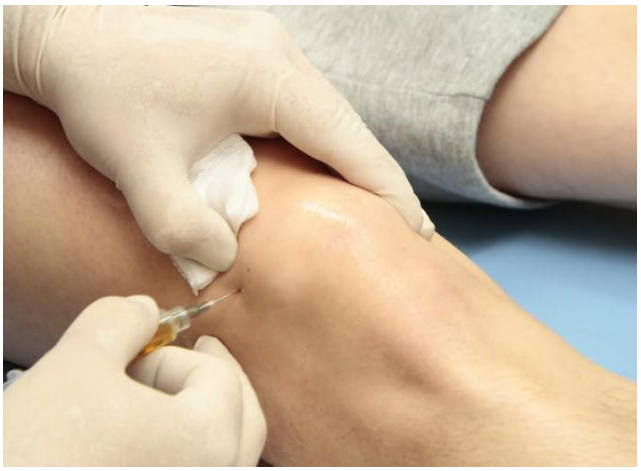

Figure 2: Administration of platelet-rich plasma (PRP) injection for knee osteoarthritis.

4.10. Ethical consideration

The study protocol was approved by the Ethical Review Committee of Tezpur Medical College and Hospital. Informed consent was obtained from all participants prior to enrolment.

5. Results

From the demographic and baseline characteristics presented in Table 1, the two groups, HA and PRP, were well-matched with no statistically significant differences observed. Both groups had a similar mean age, with Group

A (HA) averaging 55 years and Group B (PRP) at 54 years (p=0.65). The gender distribution was nearly identical between the two groups (p=0.78). Both groups also showed comparable BMI and duration of knee osteoarthritis, with p-values of 0.74 and 0.68, respectively. At the outset, patients in both groups reported similar pain and functional disability levels, as denoted by nearly identical VAS (p=0.82) and WOMAC scores (p=0.79).

The clinical assessment outcomes over time, highlighted in Table 2, demonstrated that while both treatments were effective in reducing pain and improving function, the PRP group consistently outperformed the HA group. By the 12-month mark, the PRP group's mean VAS score improved to 5.2 compared to the HA group's 6.5, with the difference being statistically significant (p=0.04). Similarly, the WOMAC score, which measures pain, stiffness, and physical function, was better in the PRP group at 50 compared to 56 in the HA group by 12 months (p=0.03).

Comparing the efficacy in Table 3, the PRP group exhibited a more significant reduction in VAS scores over time, with a 31.6% improvement by 12 months, compared to a 13.3% improvement in the HA group (p=0.04). Likewise, the WOMAC scores reduced more in the PRP group, indicating better functional outcomes with 15.2% improvement by the end of the year compared to a 6.6% improvement in the HA group (p=0.03).

Safety evaluations, as summarized in Table 4, revealed that both treatments were generally well-tolerated. However, the HA group had slightly higher incidences of injection site pain (20% vs. 12%, p=0.34) and local swelling (16% vs. 8%, p=0.29). Allergic reactions were only noted in the HA group (4%) with none reported in the PRP group, though this was not statistically significant (p=0.31).

From Table 4, assessing patient satisfaction, a significant proportion of patients in the PRP group (64%) reported being "very satisfied" with their treatment compared to only 32% in the HA group (p=0.02). Furthermore, a remarkable 92% of PRP-treated patients expressed a willingness to repeat the treatment if necessary, in contrast to 60% from the HA group (p=0.01). Both these indicators underline the perceived efficacy and acceptability of PRP over HA among the study participants.

Lastly, long-term outcomes and repeat treatments (Table 4) pointed out another advantage of PRP over HA. Only 24% of PRP-treated patients required repeat injections within the year, while this number was notably higher at 56% for the HA group (p=0.01). Moreover, on average, PRP-treated patients had a longer duration before requiring another treatment, with an average of 10.5 months compared to 7.5 months in the HA group (p=0.03).

6. Discussion

The management of knee osteoarthritis (OA) has been significantly impacted by the therapeutic potential of both Hyaluronic Acid (HA) and Platelet Rich Plasma (PRP).[19] Our study underscores the increasingly evident potential superiority of PRP over HA, which is highlighted in several domains including efficacy, safety, and patient satisfaction.

Our findings demonstrate that, by the 12-month mark, the PRP group had a significant improvement in VAS scores, reducing to 5.2 compared to the 6.5 observed in the HA group (p=0.04). This is consistent with a meta-analysis by Dai et al., which reported PRP injections as notably superior to HA injections in alleviating pain, especially over longer durations.[20] Similarly, our study indicated a statistically significant difference in WOMAC scores at 12 months between PRP and HA groups, which resonates with the results of Kon et al., where PRP showed consistent improvements in function.[21]

However, the beneficial effects of PRP might not be universal. Some studies suggest greater benefits in younger patients with earlier stages of OA.[22] This is noteworthy as it indicates potential selection criteria for PRP treatment, suggesting that not all OA patients may derive equivalent benefit.

Safety remains paramount. While our data pointed to fewer adverse reactions in the PRP group compared to HA, Filardo et al. reported that adverse reactions between the two treatments were largely comparable.[23] The discrepancy underscores the need for further standardized investigations into the safety profiles of both interventions.

Our study further emphasized patient satisfaction and longevity of therapeutic benefits. An impressive 92% of participants in our study were willing to undergo a repeat PRP treatment if needed. This high satisfaction rate aligns with a study by Görmeli et al., where PRP outperformed HA in terms of patient satisfaction and the duration of therapeutic benefits.[24]

In wrapping up, our findings, bolstered by extant literature, accentuate PRP's potential benefits over HA in knee OA management. Future endeavours should focus on standardizing PRP preparation and administration, conducting larger multicentric trials, and ensuring prolonged follow-up to foster a more definitive understanding of its role in OA management.

7. Conclusion

Our study sheds pivotal insights into the therapeutic potential of Platelet Rich Plasma (PRP) and Hyaluronic Acid (HA) in the management of knee osteoarthritis (OA). Based on the comparative analysis, PRP consistently demonstrated enhanced clinical outcomes, especially in terms of pain reduction and functional improvement as indicated by VAS and WOMAC scores. The PRP group not only showcased a significant reduction in symptoms but also maintained these improvements for a longer duration, underscoring its sustained efficacy.

Table 1: Demographic andbaseline characteristics of participants

Parameters	Group A (HA)	Group B (PRP)	p-value
Mean Age (years)	55	54	0.65
Gender (M/F)	12/13	13/12	0.78
Mean BMI	28.5	28.3	0.74
Duration of OA (years)	5.7	5.6	0.68
Baseline VAS Score	7.5	7.6	0.82
Baseline WOMAC Score	60	59	0.79

Table 2: Clinical assessment outcomes at different time points

Parameters/Time Intervals	Baseline	1 Month	3 Months	6 Months	12 Months	p-value (12 months)
Group A (HA) - VAS Score	7.5	6.0	5.8	6.2	6.5	0.04
Group B (PRP) - VAS Score	7.6	5.0	4.5	4.8	5.2	
Group A (HA) - WOMAC Score	60	53	52	54	56	0.03
Group B (PRP) - WOMAC Score	59	49	45	47	50	

Table 3: Comparativeefficacy at different time intervals

Parameters/Time Intervals	1 Month (%)	3 Months (%)	6 Months (%)	12 Months (%)	p-value (12 months)
Group A (HA) - VAS Reduction	20%	22.6%	17.3%	13.3%	0.04
Group B (PRP) - VAS Reduction	34.2%	40.8%	36.8%	31.6%	
Group A (HA) - WOMAC Reduction	11.6%	13.3%	10%	6.6%	0.03
Group B (PRP) - WOMAC Reduction	16.9%	23.7%	20.3%	15.2%	

Table 4: Comprehensive evaluation of treatment effects and patient feedback

Parameters/Safety and Satisfaction Indicators	Group A (HA)	Group B (PRP)	p-value
Safety Evaluation and Adverse Events			
Injection site pain	5 (20%)	3 (12%)	0.34
Local swelling	4 (16%)	2 (8%)	0.29
Allergic reaction	1 (4%)	0 (0%)	0.31
Patient Satisfaction Survey Results			
Overall Satisfaction - Very Satisfied	8 (32%)	16 (64%)	0.02
Willingness to Repeat Treatment - Yes	15 (60%)	23 (92%)	0.01
Perceived Improvement - Significant	9 (36%)	19 (76%)	0.03
Long-term Outcomes and Requirement for Repeat Injections			
Patients requiring repeat injections	14 (56%)	6 (24%)	0.01
Average time to requiring repeat treatment (months)	7.5	10.5	0.03

Furthermore, the safety profiles of both treatments were comparable, with minimal adverse events reported in either group. This is crucial in establishing the real-world applicability of a treatment modality, as safety often dictates clinical decision-making.

An integral aspect that stood out was the higher patient satisfaction rate with PRP. The willingness of patients to undergo a repeat PRP treatment if needed, in stark contrast to the HA group, emphasizes the perceived benefits and overall positive experience with PRP.

However, while our findings underscore PRP's potential, it's also essential to recognize the need for standardized PRP preparation and administration protocols. Variability in preparation methods might yield inconsistent results, making standardization paramount for achieving replicable outcomes.

In the light of our findings and the current literature, PRP emerges as a promising treatment modality for knee

OA. The next steps should encompass larger multicentric trials, prolonged follow-ups, and meticulous standardization protocols to ascertain PRP's definitive position in knee OA management guidelines.

8. Source of Funding

None.

9. Conflict of Interest

None.

References

1. Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage*. 2013;21(9):1145–53.
2. Goldring MB, Goldring SR. Articular cartilage and subchondral bone in the pathogenesis of osteoarthritis. *Ann N Y Acad Sci*. 2010;1192:230–7. doi:10.1111/j.1749-6632.2009.05240.x.
3. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. *Arthritis Rheum*. 2012;64(6):1697–7.
4. Peat G, Mccarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. *Ann Rheum Dis*. 2001;60(2):91–7.
5. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage*. 2008;16(2):137–62.
6. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)*. 2012;64(4):465–74.
7. Gomoll AH, Yanke AB, Kang RW, Chubinskaya S, Williams JM, Bach BR, et al. Long-term effects of bony resection via the tibial tubercle osteotomy for patellar instability. *Knee Surg Sports Traumatol Arthrosc*. 2008;16(10):917–23.
8. Laurent TC. Structure of hyaluronic acid. In: Balasz E, editor. Chemistry and molecular biology of the intercellular matrix. vol. 1. London: Academic Press; 1970. p. 703–32.
9. Smith MM, Ghosh P. The synthesis of hyaluronic acid by human synovial fibroblasts is influenced by the nature of the hyaluronate in the extracellular environment. *Rheumatol Int*. 1987;7(3):113–22.
10. Ghosh P, Guidolin D. Potential mechanism of action of intra-articular hyaluronan therapy in osteoarthritis: are the effects molecular weight dependent? *Semin Arthritis Rheum*. 2002;32(1):10–37.
11. Altman RD, Manjoo A, Fierlinger A, Niazi F, Nicholls M. The mechanism of action for hyaluronic acid treatment in the osteoarthritic knee: a systematic review. *BMC Musculoskelet Disord*. 2015;16:321. doi:10.1186/s12891-015-0775-z.
12. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? *Implant Dent*. 2001;10(4):225–8.
13. Everts PA, Knape JT, Weibrich G. Platelet-rich plasma and platelet gel: a review. *J Extra Corpor Technol*. 2006;38(2):174–87.
14. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med*. 2009;37(11):2259–72.
15. Sundman EA, Cole BJ, Fortier LA. Growth factor and catabolic cytokine concentrations are influenced by the cellular composition of platelet-rich plasma. *Am J Sports Med*. 2011;39(10):2135–40.
16. Rutjes AW, Jüni P, Costa BD, Trelle S, Nüesch E, Reichenbach S, et al. Viscosupplementation for osteoarthritis of the knee: a systematic review and meta-analysis. *Ann Intern Med*. 2012;157(3):180–91.
17. Kon E, Mandelbaum B, Buda R. Platelet-rich plasma intra-articular injection versus hyaluronic acid viscosupplementation as treatments for cartilage pathology: from early degeneration to osteoarthritis. *Arthroscopy*. 2011;27(11):1490–501.
18. Wang-Saegusa A, Cugat R, Ares O, Seijas R, Cuscó X, Garcia-Balletbó M, et al. Infiltration of plasma rich in growth factors for osteoarthritis of the knee short-term effects on function and quality of life. *Arch Orthop Trauma Surg*. 2011;131(3):311–7.
19. Campbell KA, Saltzman BM, Mascarenhas R. Does Intra-articular Platelet-Rich Plasma Injection Provide Clinically Superior Outcomes Compared With Other Therapies in the Treatment of Knee Osteoarthritis? A Systematic Review of Overlapping Meta-analyses. *Arthroscopy*. 2015;31(11):2213–21.
20. Dai WL, Zhou AG, Zhang H, Zhang J. Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Meta-analysis of Randomized Controlled Trials. *Arthroscopy*. 2017;33(3):659–70.
21. Kon E, Mandelbaum B, Buda R. Platelet-rich plasma intra-articular injection versus hyaluronic acid viscosupplementation as treatments for cartilage pathology: from early degeneration to osteoarthritis. *Arthroscopy*. 2011;27(11):1490–501.
22. Cerza F, Carnì S, Carcangiu A, Vavo ID, Schiavilla V, Pecora A, et al. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. *Am J Sports Med*. 2012;40(12):2822–7.
23. Filardo G, Kon E, Martino AD, Matteo BD, Merli ML, Cenacchi A, et al. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. *BMC Musculoskelet Disord*. 2012;13:229. doi:10.1186/1471-2474-13-229.
24. Görmeli G, Görmeli CA, Ataoglu B, Çolak C, Aslantürk O, Ertem K. Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(3):958–65.

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