



Original Article

## Comparative study of platelet-rich plasma and hyaluronic acid in osteoarthritis of knee: A clinical study

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### ABSTRACT

**Objectives:** The objective of this clinical study was to compare the effectiveness of intra-articular (IA) injections of platelet-rich plasma (PRP) with that of hyaluronic acid (HA) in people with symptomatic knee osteoarthritis (OA) over each follow-up interval.

**Material and Methods:** A randomised controlled trial included 60 patients. The National Health and Medical Research Council Clinical Trial Centre permuted a computer-generated random number sequence. After telephone, radiographic, and laboratory screening, administered three weekly IA knee injections. Blood was drawn to prevent blindness. Each weekly visit produced fresh PRP samples.

**Results:** PRP was compared to a HA in a study examining the treatment of knee OA, and the results are displayed. The two groups reported comparable levels of knee discomfort at baseline but after two months. Patients receiving PRP were likelier to report overall improvement at 12 months.

**Conclusion:** This study reveals that PRP is more effective than HA in treating patients with moderate to mild radiographic PRP-alone therapy in pain relief and function improvement for patients with Knee OA who are experiencing symptoms.

**Keywords:** Hyaluronic acid, Intraarticular, Knee pain, Osteoarthritis, Plasma, Platelets

### INTRODUCTION

Degenerative arthritis, often known as osteoarthritis (OA), affects the knees and is typically caused by articular cartilage loss and damage that develops over time. Older adults are particularly more affected. The two types of OA in the knee are primary and secondary. Deterioration of the articular cartilage caused by primary OA is an uncertain aetiology.<sup>1</sup> Secondary OA is brought on by damaged cartilage in the articular cartilage, like that found incorrect pressure transmission, notably with post-traumatic reasons, across the joint in rheumatoid arthritis (RA). OA typically progresses over time and becomes a disabling condition. Everyone's clinical signs may differ in their severity. However, as time passes, they typically worsen and occur more frequently, and worsen, becoming crippling.<sup>2</sup> Everybody advances at a different rate. Common clinical symptoms of knee include pain that gradually worsens with movement, stiffness with swelling in the knees, and discomfort after long stretches of pain that worsens with time, sitting, or resting. When non-invasive therapy are ineffective, invasive treatments are started with knee OA.<sup>3</sup> No medications are known to cause knee OA, even though conservative treatments

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can help delay the onset of RA and other inflammatory disorders. Depending on the underlying cause, knee OA can be classified as primary or secondary. Unknown causes of articular cartilage degradation lead to primary knee OA. This is frequently regarded as deterioration brought on by ageing and normal wear and tear. Articular trauma is a known cause of the articular cartilage's degradation which ultimately leads to OA in the knee joint.<sup>4</sup>

The most prevalent kind of OA, knee OA, is expected to become more widespread as life expectancy and obesity rates rise. Various sources show symptomatic knee OA affects 13% of women and 10% of men aged 60 and beyond.<sup>5</sup> When a person is above 70, the frequency rises to 40%. Additionally, men are less likely than women to have knee OA. It is noteworthy to remember that not everyone with knee OA will have symptoms. Based on one study, just 15% are symptomatic in patients with imaging evidence of knee OA. Age-related severe knee OA typically affects 240 persons per 100,000 annually.<sup>6</sup>

Because intra-articular (IA) corticosteroids' benefits last only a few weeks and repeated injections have been linked to increased cartilage loss, they are typically only recommended for temporary pain relief.<sup>7</sup> According to some publications, hyaluronic acid (HA) has dubious use. However, other authors claim that after three and five HA injections, the pain was reduced weekly for five to thirteen weeks (and occasionally up to a year).<sup>8</sup>

Recently, biological therapies like platelet-rich plasma (PRP) have been researched on how to treat OA in the knee. PRP is produced from an individual's blood. Vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor (TGF), and other compounds are thought to be released by PRP, contributing to its effectiveness.<sup>9</sup> According to certain papers, PRP has shown promise for the treatment of knee OA. However, the majority disagree as the most effective techniques and have several shortcomings that make it difficult to analyse their results properly without running the risk of bias.<sup>10</sup> For establishing ideal PRP systems, heterogeneity within published studies' preparation and administration techniques is restricted. The use of HA as a comparison in most trials is also questionable. In certain trials, PRP was compared to HA, and the results revealed that PRP dramatically improved symptoms at six and 12 months compared to HA.<sup>11</sup> However, the studies in question had numerous methodological flaws, such as improper blinding, which indicated that perhaps the benefits were exaggerated.<sup>12</sup> The benefits of PRP for treating knee OA are such as it is quick and simple preparation; it is comparatively straightforward to use, it is an extremely cheap method owing to the availability for the presence of public health service facilities and apparatus; and probable secure,

due to its nature, it constitutes an autologous product. Only minor and transient complications have been described in prior publications.<sup>13</sup>

## MATERIAL AND METHODS

### Study design

A randomised control trial was conducted on 60 patients, whose study period was January 2021 to December 2022, who came to the outpatient department. Sixty patients are included in the study, fulfilling inclusion and exclusion criteria. The National Health and Medical Research Council Clinical Trial Centre created the randomisation sequence generated by computer-randomised numbers. Then it saved it with permuted blocks with sizes of 6 or 10 segregated by site and radiological severity. The biostatistician, assessors, injecting radiologists, and participants were all blinded to the groups they were assigned to.

Before attending a study centre for clinical examination, prospective participants underwent online screening, followed by telephone, radiographic, and screening in the laboratory. Participants who met the criteria filled out baseline questionnaires and went to one of two radiology facilities for MRI. From two weeks before baseline assessment through the 24-month follow-up, individuals were instructed to stop using nonsteroidal anti-inflammatory drugs and other painkillers for knee pain (apart from 24-month follow-up).

We administered three IA knee injections (at a duration of three weeks) to those who participated in both groups, with the choice of a subcutaneous local anaesthetic injection. This procedure was performed with ultrasound assistance and a medial patellofemoral technique. To preserve blindness, blood was drawn from each subject. Each weekly visit included preparing fresh PRP samples utilising a commercial item and single centrifugation at 1500 g for 5 min. This leukocyte-poor method produces platelet concentration factors 1.6–5 times higher than whole blood values and recovers around 80% of the original platelets.

### Inclusion and exclusion criteria

Participants are required to be 50 years of age and older, have moderate to mild radiographic knee OA, have had pain in the knee on the majority of days over the previous month, and have a mean knee pain level of at least 4 in the last week on an 11-point numeric grading scale.

Radiographic joint space narrowing higher than the injection of glucocorticoids within the last three months or HA within the last six months, systemic or inflammatory disease, a platelet count of 150103/L or less, prior use of an autologous blood product or stem cell preparation, bleeding disorder,

or continuing anticoagulation medication therapy were all considered exclusion criteria.

**Statistical analysis**

Data entry and statistical analysis were done using analysis of the variance statistical software. The proper percentage comparisons between the various groups were made using the Chi-square test, the student’s *t*-test, standard deviations, and mean values. The threshold for significant data was a *P* value of 0.05.

**Ethical approval**

The authors gave the patients a full explanation of the study. The patients’ consent has been obtained. The study’s methodology has indeed been approved by the hospital’s ethical review board.

**RESULTS**

Table 1 displays the baseline characteristics of the study participants, categorised into various parameters. The table describes two groups of participants, the first column representing Group 1 and the second column representing Group 2. The mean age of the participants was 63.2 years in Group 1 and 62.1 years in Group 2, with a standard deviation of 6.7 and 6.9, respectively. Regarding sex, 58.3% and 56.7% were female in Group 1 and Group 2, respectively, while 41.7% and 43.3% were male. The table also presents the Kellgren and Lawrence grade of radiographic severity, with 46.6% and 50% of participants in Group 1 and Group 2, respectively, having a grade of 2.

In comparison, 53.3% and 50% had a grade of 3. Knee alignment was also similar in both groups. Many participants reported problems in other joints, with back problems being the most common in both groups. The use of pain medication was also noted, with 33.3% and 56.7% of participants in Group 1 and Group 2, respectively, using acetaminophen alone or in combined formulations. Physical activity and overall knee pain scores were similar in both groups. However, there were differences in medial tibial cartilage volume and medial tibial plateau cross-sectional area, with higher values in Group 2. Knee effusion was also more prevalent in Group 2 than in Group 1.

Table 2 displays the baseline and 12-month outcomes of the study participants, along with the difference in change between the two groups and their corresponding *P* values. The study compared the effectiveness of PRP with a HA group for treating knee OA. The primary outcomes included the overall knee pain score and the annual medial tibial cartilage volume change. At baseline, both groups had

**Table 1:** Baseline characteristics of participants.

Characteristic	PRP (n = 60) Group 1	Hyaluronic acid (n = 60) Group 2
Age, mean (SD), years	63.2 (6.7)	62.1 (6.9)
Sex, No. (%)		
Female	35 (58.3)	34 (56.7)
Male	25 (41.7)	26 (43.3)
Height, mean (SD), m	168.2 (10.5)	167.9 (9.8)
Weight, mean (SD), kg	82.3 (13.9)	83.6 (14.8)
Body mass index, mean (SD)	29.7 (4.1)	29.9 (4.7)
Kellgren and Lawrence grade of radiographic severity, No. (%)		
2	28 (46.6)	30 (50)
3	32 (53.3)	30 (50)
Knee alignment, mean (SD), degrees	181.0 (3.7)	181.3 (3.9)
Currently employed, No. (%)	37 (61.7)	42 (70)
Symptom duration, median (IQR), years	4.3 (1.2–10.8)	5.4 (1.7–9.5)
Unilateral symptoms, No. (%)	14 (23.3)	19 (31.7)
Problems in other joints, No. (%)		
Back	26 (43.3)	24 (40)
Hand	16 (26.7)	19 (31.7)
Neck	14 (23.3)	15 (25)
Foot	12 (20)	8 (13.3)
Shoulder	10 (16.7)	15 (25)
Hip	10 (16.7)	9 (15)
Current pain medication use, No. (%)	20 (33.3)	34 (56.7)
Acetaminophen alone or in combined formulations	16 (26.7)	33 (55)
Topical anti-inflammatory drugs	10 (16.7)	8 (13.3)
Nonsteroidal anti-inflammatory drugs	7 (11.6)	6 (10)
Oral opioids	3 (5)	3 (5)
Oral corticosteroids	2 (3.3)	2 (3.3)
Treatment expectation, No. (%)		
No effect	2 (3.3)	0 (0)
Improvement		
Minimal	5 (8.3)	4 (6.7)
Moderate	32 (53.3)	22 (36.7)
Large	16 (26.7)	17 (28.3)
Complete recovery	2 (3.3)	1 (1.7)

(Contd...)

**Table 1:** (Continued)

Characteristic	PRP (n = 60) Group 1	Hyaluronic acid (n = 60) Group 2
Pain DETECT results, No. (%)		
Nociceptive knee pain	25 (41.7)	27 (45)
Unclear	7 (11.6)	10 (16.7)
Neuropathic-like knee pain	1 (1.7)	3 (5)
Physical activity scale for the elderly score, median (IQR)	60.2 (45.5–55.9)	58.5 (40.8–36.8)
Overall knee pain score, mean (SD)	4.0 (2.5)	4.4 (0.8)
Medial tibial cartilage volume, mean (SD), mm <sup>3</sup>	216 (147)	458 (261)
Medial tibial plateau cross-sectional area, mean (SD), cm <sup>2</sup>	3.2 (4.1)	13.9 (1.8)
Presence of knee effusion, No. (%)	12 (20)	15 (25)
PRP: Platelet-rich plasma, SD: Standard deviation, IQR: Interquartile range		

similar overall knee pain scores (4.7 for the PRP group and 3.9 for the HA group). They showed significant improvement at 12 months (2.8 for the PRP group and 2.7 for the HA group). The secondary outcomes included knee pain while walking, intermittent and constant OA pain, knee injury, OA outcome score, function in daily living, function in sport and recreation, knee-related quality of life, and assessment of the quality of life-8-dimension score showed not much difference. The table presents the outcomes of participants in a clinical trial comparing the effectiveness of PRP and HA injections in treating knee OA over 24 months. The table presents the mean (SD) values of the outcomes at baseline, three, six, 12, and 24 months for the PRP and HA groups, as well as the difference in change between the groups at one year with the corresponding *P* value. The primary outcome measures included the overall knee pain score and the annual medial tibial cartilage volume change. The secondary outcome measures had knee pain while walking, constant and intermittent OA pain scores, knee injury and OA outcome score (KOOS), daily living function, sport and recreation, and knee-related quality of life. The difference in change between the PRP and HA groups was insignificant for most of the outcome measures at one year, except for the KOOS pain score and the KOOS other symptoms score, which showed a trend toward significance. The study concludes that PRP injections may not be more effective than HA injections in treating knee OA.

Table 3 reports the results of a clinical trial evaluating the efficacy of PRP compared to the HA group for treating

knee OA. The table provides information on joint structural outcomes assessed two and 12 months after treatment. At two months, 38.3% of patients receiving PRP reported improvement, compared to 33.3% in the HA group. PRP showed a trend towards improvement in pain at two months, although it did not reach statistical significance. There was a significant difference in function improvement at two months, with 35% of patients in the PRP group improving compared to 23.3% in the HA group. At 12 months, PRP was associated with a higher proportion of patients reporting overall improvement (46.7%) compared to the HA group (36.7%).

## DISCUSSION

The prospective study aimed to determine if knee OA patients may get PRP safely and effectively. To accomplish this, PRP, a substantial amount of numerous growth factors (GFs), inflammatory substances, and regulatory factors in an allogeneic blood product, has demonstrated encouraging results.<sup>14</sup> In the comparison of evaluations, visual analog scale, Knee Society Score, and Western Ontario and McMaster University Arthritis Index (WOMAC) all showed significant statistical declines (*P* < 0.05). However, magnetic resonance imaging results showed no scientific importance in the femoral or the tibial plates (*P* = 0.46 and 0.33) improvement in cartilage thickness. Even the follow-up baseline, three, six, 12, and 24 months, PRP injection is a valid conservative treatment method while enhancing functional and standard-of-life pain scores.<sup>15</sup>

OA, the most prevalent type of arthritis, significantly affects a person's mobility as well as the quality of life of the patient. Although pharmacological treatments for OA, like corticosteroids, have limited long-term efficacy, they immediately reduce the patients' discomfort and enhance their mobility and quality of life.<sup>16</sup> Due to its trophic qualities and capacity to modulate inflammatory processes, PRP is used as a therapeutic approach, particularly in musculoskeletal applications. This study aims to evaluate and contrast the therapeutic benefits of PRP compared to a HA in patients with mild to moderate knee OA symptoms.<sup>17</sup> The single PRP/HA injection into a joint is harmless. It helps to discomfort and knee function in individuals with moderate to severe symptoms of knee OA scores (with no differences between the groups that could be seen). In a two-year follow-up, PRP showed statistically significant improvement versus HA.<sup>18</sup>

In older persons, knee OA constitutes a frequent illness. A successful invasive for knee OA is PRP, administered IA. Our goal was to contrast compared to a HA group or other traditional therapies regarding PRP, effectiveness, and safety. PRP is more successful as symptom relief when

Table 2: Outcome of participants at baseline and 24 months.

Outcomes	Values, mean (SD)												Difference in change between groups, mean (95% CI)	P value
	PRP (n = 60) group						Hyaluronic acid (n = 60) group							
	Baseline	3 months	6 months	12 months	24 months	Baseline	3 months	6 months	12 months	24 months				
Primary outcomes														
Overall knee pain score	4.7 (2.9)	4.6 (2.4)	3.9 (2.2)	2.8 (2.1)	2.0 (1.9)	3.9 (0.6)	3.1 (0.4)	2.8 (1.2)	1.6 (1.9)	1.5 (1.8)	-0.3 (-0.6 to 0.3)	0.43		
Annual change in medial tibial cartilage volume, %				-1.5 (1.8)					-1.1 (4.5)		-1.7 (-1.7 to 1.2)	0.64		
Secondary outcomes														
Knee pain while walking	2.5 (1.9)	2.6 (1.8)	2.7 (1.7)	2.7 (1.7)	2.8 (1.6)	3.9 (1.8)	3.5 (1.4)	2.9 (2.6)	2.7 (2.8)	2.5 (2.9)	-0.6 (-0.3 to 0.7)	0.32		
Intermittent and constant osteoarthritis pain scored														
Constant pain	4.9 (3.8)	3.8 (3.1)	2.9 (2.0)	2.7 (2.2)	2.5 (1.9)	4.6 (1.7)	3.9 (2.5)	2.9 (4.0)	2.4 (5.2)	2.2 (5.8)	-0.6 (-4.4 to 1.9)	0.65		
Intermittent pain	09.9 (3.8)	2.9 (3.9)	3.5 (4.9)	5.8 (5.9)	5.4 (6.0)	8.9 (7.7)	7.7 (8.1)	5.6 (6.1)	4.9 (5.1)	4.0 (4.9)	-0.7 (-5.6 to 1.9)	0.55		
Knee injury and osteoarthritis outcome score														
Pain	43.2 (13.9)	48.1 (13.8)	52.2 (14.1)	57.4 (14.9)	59.0 (15.8)	13.8 (11.7)	26.8 (12.9)	39.2 (16.7)	54.5 (18.9)	56.2 (19.8)	2.3 (-0.9 to 5.2)	0.16		
Other symptoms	34.2 (15.3)	39.8 (15.3)	48.7 (15.2)	57.6 (15.2)	60.1 (16.2)	33.6 (14.9)	38.6 (15.9)	46.5 (16.9)	54.2 (18.7)	58.4 (19.8)	2.5 (-0.6 to 6.5)	0.08		
Function in daily living	38.7 (16.2)	45.6 (15.9)	51.2 (14.0)	57.6 (14.9)	59.6 (14.7)	41.9 (14.4)	44.1 (13.5)	48.5 (13.6)	51.7 (12.3)	54.5 (11.8)	0.6 (-1.8 to 4.7)	0.52		
Function in sport and recreation	12.5 (17.8)	24.6 (16.9)	40.0 (15.1)	55.6 (15.8)	58.2 (14.9)	16.5 (8.9)	22.5 (10.9)	28.0 (12.2)	31.3 (15.3)	33.2 (16.2)	1.2 (-2.3 to 6.3)	0.37		
Knee-related quality of life	22.6 (12.2)	29.5 (11.9)	35.8 (11.0)	41.5 (10.6)	43.8 (9.8)	34.6 (17.2)	35.9 (15.0)	36.8 (13.9)	38.9 (12.4)	40.5 (11.5)	2.5 (-0.6 to 5.7)	0.24		
Assessment of quality of life-8 dimension score	0.47 (0.17)	0.49 (0.18)	0.52 (0.19)	0.55 (0.19)	0.56 (0.20)	0.53 (0.19)	0.52 (0.19)	0.50 (0.19)	0.49 (0.19)	0.47 (0.18)	-0.00 (-0.04 to 0.03)	0.72		
PRP: Platelet-rich plasma, CI: Confidence interval, SD: Standard deviation														

**Table 3:** Global improvement and other joint structural outcomes.

Outcomes	No./total (%)		Absolute difference (95% CI)	Risk ratio (95% CI)	P value
	Platelet-rich plasma (n = 60)	Hyaluronic acid (n = 60)			
Global change at 2 months					
Improved overall	23 (38.3)	20 (33.3)	11.12 (1.19–14.09)	2.45 (0.12–0.89)	0.05
Improved pain	27 (45)	24 (40)	16.09 (–0.19 to 22.21)	1.22 (0.73–6.23)	0.09
Improved function	21 (35)	14 (23.3)	4.58 (–4.32 to 15.49)	0.19 (0.59–0.67)	0.24
Global change at 24 months					
Improved overall	28 (46.7)	22 (36.7)	7.43 (–0.41 to 18.54)	0.19 (0.18–0.18)	0.17
Improved pain	20 (33.3)	21 (35)	10.26 (–0.21 to 11.48)	0.37 (0.65–1.69)	0.05
Improved function	24 (40)	14 (23.3)	10.23 (0.18 to 21.17)	0.18 (2.12–2.19)	0.07
MRI osteoarthritis knee score sub scores at 24 months					
Worse meniscus morphology	10 (16.7)	15 (25)	–1.21 (–11.20 to 7.23)	0.89 (0.59–2.17)	0.70
Worse intercondylar synopsis	4 (6.7)	7 (11.6)	–2.17 (–9.71 to 1.59)	0.56 (0.28–0.27)	0.67
No. of areas of cartilage thinning					
0	37 (61.6)	40 (66.7)	-	2.2	
1	12 (20)	16 (26.7)	-	0.74 (0.42–1.26)	0.34
2	7 (11.7)	6 (10)	-	1.23 (0.52–1.23)	0.66
≥3	10 (16.7)	3 (5)	-	1.68 (0.41–5.54)	0.02
Change in whole knee effusion					
Improved	8 (13.3)	14 (23.3)	-	0.71 (0.32–0.39)	0.87
No change	30 (50.0)	34 (56.7)	-	1.2	
Worsened	12 (20)	8 (13.3)	-	0.84 (0.18–1.55)	0.7
Other MRI measures at 24 months					
Bone marrow lesion progression	8 (13.3)	10 (16.7)	2.62 (–3.14 to 12.19)	0.29 (1.25–0.21)	0.25
Cartilage defects progression	8 (13.3)	6 (10)	5.21 (–0.99 to 12.21)	0.48 (0.19–1.84)	0.57

CI: Confidence interval, MRI: Magnetic resonance imaging

compared to the above-stated treatments. The short-term therapeutic effects of triple PRP therapy and single PRP application were comparable.<sup>19</sup>

To examine the impact, a randomised clinical trial with a control group was conducted to investigate the benefits of PRP on knee OA sufferers’ discomfort, stiffness, and quality of life.<sup>20</sup> Two groups of patients were randomly assigned.<sup>21</sup> Both at baseline and six months after therapy, each subject completed the SF-36 questionnaire in Farsi and the WOMAC. Study subjects included both the group receiving PRP and the control group. Each contained 60 patients.<sup>22</sup> The Short Form-36’s mean changes for the total WOMAC, a summary of the physical and mental components. That study showed that PRP group participants performed better than HA. The findings of the present investigation indicate that systemic-articular PRP knee injection paired with physical

therapy can be more efficient in reducing pain, reducing stiffness, and improving quality of life than therapeutic exercise alone.<sup>23,24</sup>

Another study showed that, up to 12 months after the injection, PRP therapy produces notable clinical benefits in individuals with knee OA symptoms. Three until 24 months following the injection, PRP significantly outperforms HA results of WOMAC scores. The present study has insufficient data to compare PRP with steroids or PRP with more leukocytes versus fewer leukocytes.<sup>24,25</sup>

The goals of the study were to (1) summarise providing PRP and HA on knee OA patients, (2) identify which meta-analysis offers the strongest support for advising PRP as a component of treatment for KOA patients, and (3) note any gaps in the literature warrant further study. There is no variation in pain alleviation and improved function when

treating knee osteoarthritis patients; IA PRP injection outperforms HA in terms of risk for an adverse event over a brief period (two years).<sup>26</sup>

This study reveals that PRP is more effective than HA in treating patients with moderate to mild radiographic PRP-alone therapy in pain relief and function improvement for patients with knee OA who are experiencing symptoms.

## CONCLUSION

The study has concluded IA injections of PRP are more effective than HA among individuals with symptomatic moderate to mild radiographic knee OA. These results contradict the utility of PRP in the treatment of knee OA. The primary drawback of this study is the heterogeneity and need for more effective standardisation of PRP preparations. The trial's findings are applied to different PRP formulations. Individuals with moderate to mild radiographic knee OA were included in this study because prior research suggested that they would benefit more from PRP. The findings presented here may apply to diseases with more severe symptoms. Future studies need to be conducted to know the use of PRP in the management of OA.

**Ethical approval:** The study's methodology has been approved by the hospital's ethical review board.

**Declaration of patient consent:** Patient's consent not required as patients identity is not disclosed or compromised.

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