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Efficacy and Clinical Outcomes of Intra-Articular Injection of Platelet-Rich Plasma Versus Hyaluronic Acid for Knee Osteoarthritis

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ABSTRACT

Background: Platelet-rich plasma (PRP) and hyaluronic acid (HA) have received considerable consideration as good potential nonsurgical treatment options for knee OA.
Aim of The Work: To examine the effectiveness of PRP and HA injections in the treatment of knee OA.
Patients and Methods: In this prospective randomized clinical study, Three weekly intra-articular injections were given to 40 individuals with knee OA (20 had PRP and 20 had HA). Clinical evaluations were conducted prior to and four weeks after the third injection. In every evaluation, goniometer-measured knee flexion ROM, Western Ontario and McMaster University (WOMAC) OA index, and pain assessment using the visual analogue scale (VAS) scores were calculated.
Results: At the four-week follow-up, Active knee ROM rose from 90 ± 9.32 to 97.5 ± 9.8 (P = 0.0002) in the HA group and from 93 ± 9.67 to 102.25 ± 7.34 in the PRP group (P = 0.0000). Both groups' VAS pain and WOMAC subscale scores were considerably lower at the four-week follow-up (P = 0.001). The difference between the two groups was not statistically significant in terms of WOMAC subscale scores. However, a statistically significant improvement in VAS pain scores in the PRP group compared to the HA group was noted (P<0.05).
Conclusion: Both intra-articular PRP and HA injections for knee OA improved clinical outcomes. However, individuals who received intra-articular PRP injections had a higher likelihood of pain relief at 4 weeks than those who received intra-articular HA injections.

Keywords: *Osteoarthritis;Western Ontario and McMaster University ; Platelet-rich-plasma; Hyaluronic-acid.*

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INTRODUCTION

Osteoarthritis (OA) of the knee joint is by far the most prevalent rheumatic disorder, and it is a primary cause of functional impairment in the elderly [1,2]. The characteristic abnormalities include articular cartilage degeneration and whole-joint failure [3,4]. As a result, cartilage begins to deteriorate and deep clefts are formed. At the same time, the subchondral bone undergoes pathological changes, including the formation of subarticular cysts and osteophytes development [5]. These abnormalities cause joint dysfunction and pain, making standing, walking, and performing daily tasks difficult. They also have a significant negative impact on one's quality of life and psychological well-being. [6,7]

Despite the fact that there are various therapeutic available options, conservative treatment measures such as weight reduction, exercise, and nonsteroidal anti-inflammatory medications are only beneficial for individuals with early knee OA; advanced knee OA patients, on the other hand, are more likely to require a total knee replacement. [8,9]

Intra-articular injections of hyaluronic acid (HA) or corticosteroids (CS) have been used as conservative therapies for mild KOA for many years. [10]

Earlier studies have shown that HA improves the viscoelasticity and mechanical properties of synovial fluid or promotes endogenous HA production in both chondrocytes and synoviocytes. [11-13]

Fresh leukocyte-poor PRP is a promising new growth factor created by centrifuging autologous whole blood and separating plasma with a high platelet count (14–16). PRP has long been used to treat bone, cartilage, and soft tissue [17], and it is now increasingly being employed in orthopaedics and sports medicine [18]. However, there is disagreement on whether PRP injections should be used [6]. As a result, we are conducting this research to assess the short-term effects and clinical outcomes of PRP and HA intra-articular injections for the treatment of knee OA.

PATIENTS AND METHODS

This prospective randomised clinical study included 45 patients with knee OA, of whom 40 were eventually enrolled and 5 did not fit the requirements for inclusion. Figure 1 displays a flowchart of the study. Patients were recruited from rheumatology and rehabilitation outpatient clinics at Al-Azhar University Hospitals. This study was approved by the Research Ethics Committee of the Rheumatology and Rehabilitation Department at Al-Azhar University Hospitals, and all patients signed a written informed consent before entering the study. It is in accordance with the Helsinki Declaration's legal principles. The privacy of all details of patients was granted, as each medical file containing all inquiries contained a code number.

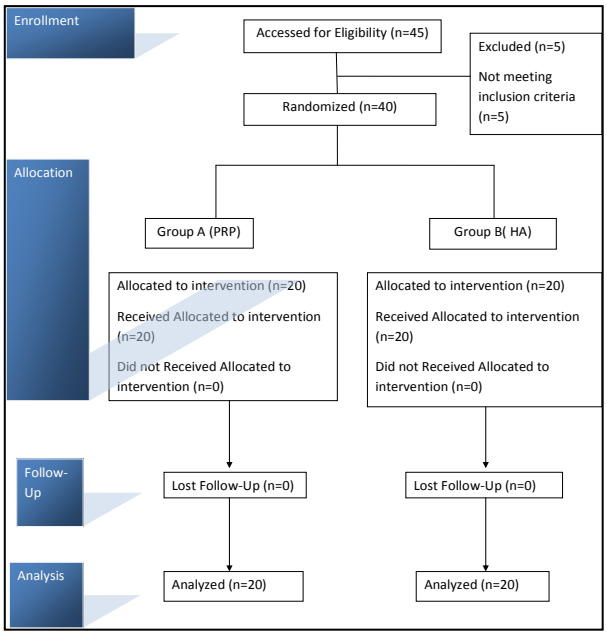

Fig. 1: Flow chart of the study subjects.

The participants were separated into two groups: 20 had intra-articular injections of autologous fresh leukocyte-poor PRP at various concentrations, whereas 20 received low molecular weight HA intra-articular injections (Hylans).

The inclusion criteria were age 40–70 years old, a history of knee pain for at least one month, a requirement for analgesics, and radiographic evidence of knee osteoarthritis (Kellgren-Lawrencegrade 1–3) (19) in which Grade 1 shows questionable narrowing of the joint space , Grade 2 shows definite osteophyte formation, and Grade 3 shows definite narrowing of the joint space with some sclerosis. Exclusion criteria included a history of diabetes or connective tissue disorders, neoplasms, platelet abnormalities, coagulation disorders, and intra-articular steroid injection within the previous six months.

Method of PRP Preparation

8.5 mL of the patient's venous blood was taken by venipuncture and mixed with 1.5 mL of anticoagulant citrate dextrose solution in a sterile vacationer. A unit (3ml) of PRP was produced after two centrifugations (one at 1200 rpm for 15 minutes to separate erythrocytes and one at 1200 rpm for 10 minutes to concentrate platelets). All of the operations were carried out at the same appointment (20)

Within half an hour, one unit of PRP was transferred to the laboratory for platelet concentration determination, while the remaining two units were used for injection. The total number of platelets per mL in PRP can be up to ten times greater than in whole blood. The skin was sterilely prepared before infiltration with an 18-gauge needle in a typical lateral approach. Following the operation, the patient was instructed to repeatedly flex and extend the leg to allow the PRP to disperse all over joint before changing into a gel (21). Patients were instructed to contact their referring physician if they experienced any side effects from the treatment. The injections, however, were safe, with no adverse reactions reported after the injection.

Hyaluronic acid

Hylans are hyaluronan (sodium hyaluronate) derivatives made up of repeating disaccharide units of N-acetylglucosamine and sodium glucuronate. Synvisc (Hylans) comes in prefilled 2-mL syringes containing hylan A with an average molecular weight of 6 million daltons. The suggested injection regimen is one injection per week for three weeks, using a syringe with a gauge of 18 to 22.

There are several methods for injecting a knee joint. One approach is to inject the knee in an extended position with the needle directed beneath the patella. In individuals who are sensitive to iodine derivatives, a topical antiseptic such as povidone-iodine is given to the region and allowed to dry before wiping away the excess with an alcohol swab. For local anaesthetic, an ethyl chloride spray was used. For the knee injection, a 1.5-inch, 22-gauge needle was utilised. If there was any resistance, the needle might need to be redirected.Following the procedure, the injected knee joint should be rested for one to two days.

Outcome Measures

At baseline, we collected demographic data, clinical features, and the Kellgren-Lawrence grading of knee OA. Further measurements were taken at the beginning and four weeks following the third injection including the subjective VAS, which is self-rated pain intensity at the time of the assessment expressed on a 10-cm horizontal scale, with 0 cm indicating "no pain" and 10 cm indicating "worst pain" (22). The Western Ontario and McMaster Universities (WOMAC) OA index is a multidimensional self-assessment questionnaire that assesses 17 functional activities, 5 pain-related activities, and 2 joint stiffness categories in three distinct subscales (23). The degree of knee flexion was determined by measuring the active range of motion of the knee with a goniometer. The standard ROM is 135° (24).

Statistical Analysis:

The sample size was calculated using data from a previous study conducted by *Raeissadat et al.* (25), who reported a success rate defined as a WOMAC total score reduction of more than 30% at the 12th month compared to the baseline. The total score reduction of WOMAC values in the PRP and HA groups was 72.5% and 22.4%, respectively. A minimum sample size of 36 patients was required for a power of 0.80 and an alpha error of 0.05. The sample size was calculated using G*Power, Version 3.1.9.2 for Windows.

A blinded medical statistics specialist input the pre/post-treatment data into the computer and then analysed it using Epi-info software, version 6.04.

RESULTS

Our study comprised 40 people who had knee osteoarthritis (20 injected with PRP and 20 with HA). There was no difference between the two groups in terms of age, gender, or affected side. The characteristics of the research subjects were shown in Table 1.

		PRP		HA		
		No.	%	No.	%	P-value
Sex	Female	14	70.0%	13	65.0%	0.596
	Male	6	30.0%	7	35.0%	
Age	Mean ± SD	55.71 ± 4.39		54.59 ± 4.54		0.057
	Range	48.0 – 67.0		45 – 66		
Side	Left	9	45.0%	10	50.0%	0.462
	Right	11	55.0%	10	50.0%	

Table 1: The initial characteristics of the study subjects.

The knee range of motion was measured by a goniometer, the VAS for pain, and WOMAC scores were assessed in our patients at baseline and 4 weeks after the intra-articular injection.

The Knee ROM measured in degrees by a goniometer shown in Table 2 revealed no statistically significant difference between the two groups either at baseline or the 4 weeks post-injection follow up (P>0.05) as.

ROM	PRP group(20)	HA group (20)	t test	P value
Baseline	93±9.67	90±9.32	1.11	0.2734
Post injection	102.25±7.34	97.5±9.8	1.73	0.0908
Difference between post & pre injection	9.25±5.2	7.5±7.35	0.86	0.3899
P value of difference	0.0000	0.0002		
% of change	10.18%	8.73%	0.60	0.5497

Table 2: Knee ROM in degrees before and after injection for cases in the PRP & HA groups.

There were highly statistically significant differences regarding knee ROM in each group. In the PRP group, ROM increased from 93 ± 9.67 to 102.25 ± 7.34 at 4 weeks with a difference of 9.25±5.2 (95 % CI, 9.25±2.279; P<0005). In the HA group, a significant increase in knee ROM from 90 ± 9.32 to 97.5 ± 9.8 was also noted with a difference of 7.5±7.35 (95 % CI, 7. 5±3.3; P<0001).

Despite the difference in knee ROM between the 4 weeks' follow-up and baseline injection in each group being highly significant, comparing these differences between the two groups showed no statistical significance (P>0.05).

A similar pattern was seen in the VAS score as shown in Table 3, which revealed a significant reduction from (8.7 ± 1.92 and 8 ± 1.03) at baseline to (4.1 ± 1.71 and 4.55 ± 1.64) at 4 weeks of follow-up in the PRP and HA groups, respectively.

VAS	PRP group(20)	HA group(20)	t test	P value
Baseline	8.7±1.92	8±1.03	1.44	0.1589
Post injection	4.1±1.71	4.55±1.64	0.84	0.4011
Difference between post & pre injection	-4.6±1.79	-3.45±1.54	2.18	0.0355
P value of difference	0.0000	0.0000		
% of change	-53.72%	-43.27%	1.73	0.0914

Table 3: VAS scale before and after injection for cases in PRP and HA groups.

The difference in VAS score between the two groups was still statistically significant (PRP vs. HA,-4.6 ± 1.79:-3.45 ±1.54) (t test = 2.18, P < 0.05) showing that the PRP injection group had a higher mean.

There were no statistically significant differences between the two groups at baseline and after 4 weeks post-injection in terms of pain, stiffness, and function subscales of the WOMAC index (Tables 4 - 6). By considering P values of mean difference (4 weeks follow-up and baseline evaluation) within each group, there were considerably better success rates in pain, knee stiffness, and physical function scores. However, the differences in WOMAC subscales between the two groups were not significant (P < 0.05).

Pain	PRP group(20)	HA group(20)	t test	P value
Pre injection	12.8±4.65	13.4±2.38	0.46	0.6433
Post injection	5.55±3.27	6.55±3.69	0.91	0.3701
Difference between post & pre injection	-7.25±3.69	-6.85±2.08	0.42	0.6757
P value of difference	0.0000	0.0000		
% of change	-58.55%	-48.3%	0.82	0.3642

Table 4: Pain scale of WOMAC index before and after injection for cases in PRP and HA groups.

Stiffness	PRP group(20)	HA group(20)	t test	P value
Pre injection	4.85±1.89	4.95±1.05	0.21	0.8378
Post injection	2.2±1.36	2.95±1.43	1.69	0.0977
Difference between post & pre injection	-2.65±1.14	-2±0.86	1.94	0.0682
P value of difference	0.0000	0.0000		
% of change	-53.98%	-42.65%	1.82	0.0761

Table 5: Stiffness subscale of WOMAC index before and after injection for cases in PRP and HA groups.

Physical function	PRP group(20)	HA group(20)	t test	P value
Pre injection	41.6±12.86	42.5±8.88	0.25	0.7981
Post injection	17.85±9.23	21.05±9.33	1.09	0.2824
Difference between post & pre injection	-23.75±7.88	-21.45±8.33	0.89	0.3752
P value of difference	0.0000	0.0000		
% of change	-59.44%	-51.01%	1.69	0.1001

Table 6: Physical function subscale of WOMAC index before and after injection for cases in HA and PRP groups:

DISCUSSION

According to the current data, PRP and HA were beneficial in terms of enhancing ROM as well as lowering VAS and WOMAC subscale scores.

Previous research has established that PRP has a beneficial impact on chondrogenesis and mesenchymal stem cell proliferation and may promote a healing response by improving the metabolic capabilities of damaged components [26]. Patel and Dhillon [27] demonstrated that PRP-induced chondral remodelling may improve tissue repair and alter inflammatory mechanisms by suppressing the NFkB signalling pathway [28, 29], which contributes to the development of OA. [8]

The great effects of HA could also be ascribed to the enhanced intra-articular environment and greater transient lubrication brought on by viscoelasticity. Moreover, the differentiation and proliferation of chondrocytes, the regulation of collagenase synthesis, and cartilage regeneration are all significantly influenced by growth factors generated by active platelets [30]. Numerous clinical studies have also demonstrated that HA increases joint mobility while reducing joint discomfort [31, 32].

There is still disagreement over which injection has the better outcome. In this study, we found that there was no difference between patients who received PRP or HA injections for the treatment of knee OA in terms of WOMAC subscale scores or knee ROM; however, PRP was better than HA in terms of VAS pain scores, indicating that intra-articular PRP injection may be more effective in relieving pain.

In accordance with our results, Filardo et al. [33] demonstrated that, while both groups showed clinical improvement at the follow-up examination, there was no statistically significant difference in the scores tested.

According to our findings, multiple studies comparing PRP and HA injections indicated that PRP was superior to HA in terms of pain relief for patients with knee OA [34- 36].

In a study done by Sánchez et al. [37] they reported that the efficacy rates for assessing pain scale at the fifth week of follow-up after the last injection were 33.43% for PRP and 10% for HA.

Another study showed that PRP is safe, considerably more effective than HA in primary and secondary outcomes, and provides a significant therapeutic benefit by reducing pain in patients with knee OA compared to baseline levels [38].

On the other hand, Montaez-Heredia et al. [39] demonstrated that there were no statistically significant differences between PRP and HA treatment for pain relief in knee osteoarthritis patients.

When considering the results of studies that contradict our findings several issues need to be addressed in relation to the PRP's effectiveness. The preparation procedures may have contributed to the variations in the results. Additionally, despite the similarities in their names, there are several procedures and concentrations that produce a variety of end products [40]. Therefore, the ability to successfully convert a harmful joint environment into a repairing or regenerating state depends largely on the concentration of platelets, leukocytes, and growth factors (30).

Limitations:

Our study's first drawback was the absence of a placebo group, which would suggest that there isn't conclusive evidence that PRP works on degenerated cartilage. Another drawback of our study was the inability to blind individuals due to PRP acquisition using blood samples collected from patients.

Although unethical, it was also possible to gather blood samples and then discard them in the group that will get HA injection. It is also worth noting that a lack of standardisation techniques during PRP preparation, as well as a variable concentration of the end product, may have an influence on the outcomes.

CONCLUSION

The study's findings revealed that the PRP and HA groups did not significantly differ in terms of increased ROM and improved WOMAC subscales score at the short-term follow-up. The VAS pain score, on the other hand, demonstrates a significant difference. As a result, PRP appears to be more effective in relieving pain. More study is needed to identify the best injection dose, frequency, and long-term follow-up effects of PRP injection in knee OA patients.

Conflict of interest : none

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