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Intra-Articular Platelet-Rich Plasma Injections VS Hyaluronic Acid for Patients with Knee Osteoarthritis: A Systematic Review

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ABSTRACT

Introduction One of the most common conditions leading to impairment, particularly in the elderly, is osteoarthritis (OA). Most often caused by knee and/or hip OA, OA is the most prevalent articular disease in the developed world and a major contributor to chronic. OA is recognized as a major contributor to disability and impairment, and it has a significant socioeconomic cost due to medical and surgical procedures, as well as lost productivity. OA is a complex chronic illness that begins with joint cartilage disintegration and progresses to synovitis, subchondral sclerosis, and the development of peripheral osteophytes. A treatment option for osteoarthritis cartilage injuries is platelet-rich plasma (PRP) therapy, which is linked to a decrease in tissue inflammation. However, there is still a lack of clinical research on PRP administration's price, length of treatment, and possible application as a treatment for articular cartilage injuries.

Objectives This study aimed to examine the clinical outcomes of patients with knee osteoarthritis, comparing the clinical results of The Western Ontario and McMaster Universities Arthritis Index (WOMAC) between PRP and HA intra-articular injection.

Methods The medical term “PRP”, “HA”, and “Knee Osteoarthritis” were used in Pubmed and Google Scholar to discover studies of the efficacy of Intra-articular PRP injection VS HA in decreasing WOMAC scores up to October 2023. Two independent reviewers excluded the non-RCTs and other clinical studies irrelevant to the study question. Seven remaining studies were reviewed and screened for inclusion based on relevance to the subject and outcomes.

Results Based on seven studies in this review, two studies showed that intra-articular platelet-rich plasma has a superior outcome on decreasing the WOMAC score than intra-articular hyaluronic acid injection with significant. Five of seven studies demonstrated that PRP has better outcomes on WOMAC score, even if not significantly.

Conclusions PRP intra-articular injection is a clinically meaningful improvement for patients with knee OA, with no significant difference between treatment groups.

KEYWORDS: *PRP, Hyaluronic Acid, Knee Osteoarthritis*

ARTICLE DETAILS

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INTRODUCTION

One of the most common conditions leading to impairment, particularly in the elderly, is osteoarthritis (OA). Most often caused by knee and/or hip OA, OA is the most prevalent articular disease in the developed world and a major contributor to chronic disability (Heidari and MD, no date). OA is recognized as a major contributor to disability and impairment, and it has a significant socioeconomic cost due to medical and surgical procedures, as well as lost productivity (Serag and Mostafa, 2020). OA is a complex chronic illness that begins with joint cartilage disintegration and progresses to synovitis, subchondral sclerosis, and the development of peripheral osteophytes (Tavassoli *et al.*, 2019). A treatment option for osteoarthritis cartilage injuries is platelet-rich plasma (PRP) therapy, which is linked to a decrease in tissue inflammation. PRP is created by centrifuging autologous blood to allow growth factors to be released from platelet granules. By altering the intra-articular

milieu, these growth factors may promote an anabolic, analgesic, and anti-inflammatory response (Paget *et al.*, 2021). Platelet-rich plasma (PRP) is rich in anti-inflammatory and anabolic proteins and has been shown to induce chondroprotection, leading to its use for the treatment of degenerative conditions such as OA (Baria *et al.*, 2022). However, there is still a lack of clinical research on PRP administration's price, length of treatment, and possible application as a treatment for articular cartilage injuries. Knee osteoarthritis (OA) is a disease with a high prevalence in the adult population (Lin *et al.*, 2019). Every day, orthopedic surgeons face the problem of osteoarthritis (OA), with a prevalence increasing day after day. Moreover, this disease has a devastating impact on a patient's quality of life and it has become the most common degenerative joint disorder in the elderly (Lin *et al.*, 2019). In recent years, viscosupplementation has been used as a therapeutic modality for the management of knee OA. The principle of viscosupplementation is based on the physiological properties of the hyaluronic acid (HA) in the synovial joint. Despite a sound principle and promising in vitro studies, clinical studies have been less conclusive on the effectiveness of HA in managing osteoarthritic knee pain (Coll *et al.*, 2013).

OBJECTIVES

This study aimed to examine the clinical outcomes of patients with knee osteoarthritis, comparing the clinical results of The Western Ontario and McMaster Universities Arthritis Index (WOMAC) between PRP and HA intra-articular injection.

MATERIAL AND METHODS

Inclusion and Exclusion Criteria

The medical term "PRP", "HA", and "Knee Osteoarthritis" were used in Pubmed and Google Scholar to discover studies of the efficacy of Intra-articular PRP injection VS HA in decreasing WOMAC scores up to October 2023. Two independent reviewers excluded the non-RCTs, article review and other clinical studies irrelevant to the study question. Seven remaining studies were reviewed and screened for inclusion based on relevance to the subject and outcomes.

Screening

After initial identification of titles and abstracts, 11000 articles were obtained from Google scholar, and from PubMed acquired 599, the total result articles were 11.599. The research was screened by title and abstract, and then 497 articles were obtained. The researcher reviewed the full-text category. 447 journals were excluded because they did not meet the requirements. 50 remaining journals were reviewed in full, and 43 were excluded because they were not eligible for inclusion criteria. In the final stage, 7 remaining studies were reviewed and screened for inclusion based on relevance to the subject and outcomes.

Review Literature Methods

The selection process had several stages: In the first stage, the results were screened for eligibility according to the inclusion and exclusion criteria. In the second stage, related to inclusion criteria, we selected peer-reviewed journal original research articles published between 2016 and 2023, written in English. Journals published in unknown databases, Publications that are not original, such as letter editors, abstract only, and editorial, were excluded from the study. The selection and refining of the studies using the PRISMA 2009 flow diagram. Excluded records were considered methodologically of a lower quality according to the subjective opinions of the reviewers. The main focus of this systematic review is the efficacy efficacy of Intra-articular PRP injection vs HA in decreasing WOMAC score. To optimize this interpretation, we will first clarify the findings. The search flow is summarized in Figure 1 article searh process.

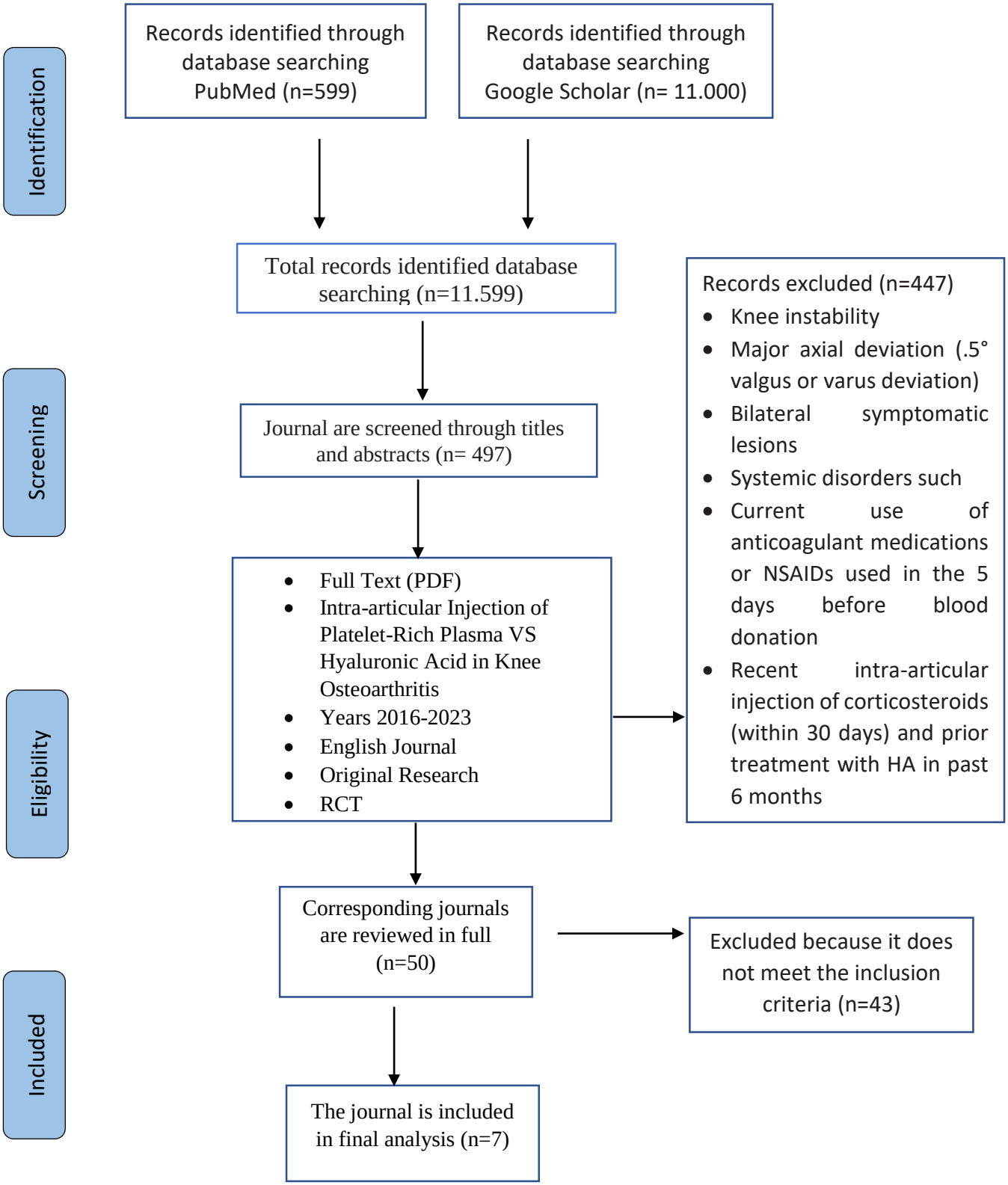

Figure 1. Article Search Process

Methodological Characteristics

Based on the Seven studies reviewed, All studies used the RCT method (López *et al.*, 2019), (Lin *et al.*, 2019), (Ying-Chun Wang, 2022), (Park, Kim and Ha, 2021), (Yavari, 2020), (Cole *et al.*, 2016), (Li *et al.*, 2021).

Intervention Methods

Out of the seven studies, seven studies used used two group random control trial (López *et al.*, 2019), (Lin *et al.*, 2019), (Ying-Chun Wang, 2022), (Park, Kim and Ha, 2021), (Yavari, 2020), (Cole *et al.*, 2016), (Li *et al.*, 2021).

RESULTS

Of 11.599 records initially identified, two studies showed that intra-articular platelet-rich plasma has a superior outcome on decreasing the WOMAC score than intra-articular hyaluronic acid injection with significant analysis P<0.05 (Yavari, 2020), (López et al., 2019). Five of seven studies demonstrated that PRP has better outcomes on WOMAC score, even if not significantly P>0.05 (Lin *et al.*, 2019), (Ying-Chun Wang, 2022), (Park, Kim and Ha, 2021), (Cole *et al.*, 2016), (Li *et al.*, 2021).

Table 1. Study of Effect of PRP VS HA Toward its Outcome

No	Study	Intervention/ Comparison	Subject Knee OA (Grade KL, I-III)	Follow-up	WOMAC Scale Baseline			WOMAC Last Follow-Up			*P-Value*
					Pain	Stiffness	Physical Function	Pain	Stiffness	Physical Function	
1.	(Lópe et al., 2019) Randomized controlled trial (Spain)	Single PRP injection	36	52 Weeks	6.09 ± 1.4	4.12 ± 0.7	32.36 ± 5.9	4.84 ± 0.7	3.45 ± 0.5 −	26.21 ± 0.8	*P<0.05*
		Single hyaluronic acid injection	33		4.12 ± 0.7	4.06 ± 1.2	32.53 ± 7.1	32.65 ± 0.7	4.27 ± 0.45	32.78 ± 0.73	
2.	(Lin KY et al., 2019) Randomized controlled trial (Taiwan)	3 Weekly PRP injection	31	12 Months	52.81 ± 18.14			63.71 ± 20.67			*P>0.05*
		3 Weekly hyaluronic acid injection	29		52.67 ± 18.06			49.33 ± 21.51			
3.	(Ying-Chun Wang, 2022) Randomized controlled trial (Taiwan)	Single PRP injection	58	6 Months	4.20 ± 0.42	1.89 ± 0.19	12.65 ± 1.38	−1.33 ± 0.41 ; P< 0.001	−0.52 ± 0.18; P< 0.004	−2.50 ± 1.15; P< 0.029	*P=0.998*
		Single hyaluronic acid injection	58		4.38 ± 0.43	1.73 ± 0.21	12.13 ± 1.27	−1.59 ± 0.40; P<0.001	−0.43 ± 0.18; P<0.013	−2.34 ± 1.17; P<0.044	
4.	(Park, Kim and Ha, 2021) Randomized controlled trial (South Korea)	Single PRP injection	55	6 Months	7.8 ± 6 3.6	3.2 ± 1.6	27.6 ± 11.3	1.9 ± 3.2	0.5 ± 1.8 9.7	4.0 ± 13.4	*P=0.967*
		Single hyaluronic acid injection	55		6.5 ± 2.8	2.9 ± 1.4	23.7 ± 8.2	1.7 ± 2.9	0.4 ± 1.7	4.4 ± 8.6	
5.	(Yavari, 2020) Randomized controlled trial (Iran)	3 Weekly PRP injection	50	12 Months	8.25± 2.7	2.86 ±1.8 2.57	30.75±8 .5	5.47±2. 6	1.8 ±1.34	19.82±8 .9	*P=0.02*
		3 Weekly hyaluronic acid injection	52		8.14 ±2.6 2.86	2.57 ±.1.4 30.75±8.5	29±8.1	6.3±2.6	1.2±1.2	24.43 ±8.4	
6.	(Cole *et al.*, 2016) Randomized controlled trial (USA)	3 Weekly PRP injection	50	12 Months	7.00 ± 0.53	NR	NNR	3.02 6 0.48	NR	NR	*P>0.05*
		3 Weekly hyaluronic acid injection	49		7.52 ± 0.58			4.00 6 0.60			
7.	(Li *et al.*, 2021) Randomized controlled trial (China)	3 Weekly PRP injection	42	6 Months	62.09±8.74			27.14±4.66			*P>0.05*
		3 Weekly hyaluronic acid injection	44		65.28±3.49			28.00±4.55			

Abbreviation: WOMAC, Western Ontario and McMaster Universities Arthritis Index; PRP, Platelet-Rich Plasma.

DISCUSSION

In total, the systematic review obtained seven articles that were relevant to the subject and outcomes. Based on research results López et al., 2019 study concluded that at the 52-week follow-up, PRP injections are superior to HA injections or oral NSAID medication in terms of clinical improvement in individuals with knee osteoarthritis. Lin et al., 2019 findings, in individuals with mild to severe osteoarthritis of the knee, intra-articular injections of PRP can result in clinically significant functional improvement for at least a year. The Ying-Chun Wang 2022 study demonstrated that there are no between-group differences at 1-, 3-, or 6-month follow-ups and that PRP and HA can significantly improve WOMAC ratings. Based on Park, Kim and Ha, 2021 study showed that compared to HA, PRP was more clinically effective. Patients in the PRP group with clinical outcomes above the minimal clinically important difference (MCID) were found to have high concentrations of growth factors. These results suggest that future research on PRP in knee osteoarthritis must consider growth factor concentration. Yavari's 2020 study showed that in addition to considerably higher satisfaction in the PRP group, there was statistically significant improvement in the VAS score and the Lequesne global, pain, and ADL scores after 12 months of injection in the PRP group compared to the HA group. Cole et al. 2016 study demonstrated no difference between HA and PRP at any point in the primary outcome measure: the patient-reported WOMAC pain score. Significant improvements were seen in other patient-reported outcome measures, with results favoring PRP over HA. Preceding a significant difference in subjective outcomes favoring PRP, there was a trend toward a decrease in 2 pro-inflammatory cytokines, suggesting that the anti-inflammatory properties of PRP may contribute to improving symptoms. In Li et al., 2021 study, These preliminary findings showed that PRP injections could considerably enhance clinical outcomes in individuals with knee OA after six months, but PRP was not more effective than HA. Compared to HA, PRP was also linked to higher incidence rates and more severe post-injection discomfort and swelling. However, these reactions were self-limiting and did not require additional treatment.

LIMITATION

The inhomogeneity of the data outcome is the study's main flaw. These limitations prevented the author from doing a meta-analysis. Another drawback of this research is the requirement to evaluate long-term impacts.

CONCLUSIONS

PRP intra-articular injection is a clinically meaningful improvement for patients with knee OA, with no significant difference between HA groups. To investigate this issue, however, more research is required.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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