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PLATELET-RICH PLASMA INJECTIONS FOR HIP OSTEOARTHRITIS: A SYSTEMATIC REVIEW

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Abstract

Osteoarthritis (OA) is the most prevalent type of joint disorder. Symptomatic hip OA was observed in 9.2% of adults aged 45 and above, with 27% displaying radiographic evidence of the condition. While there is no definitive cure for OA, numerous research studies have explored the application of PRP (Platelet-Rich Plasma) for addressing knee OA, there is a relatively limited number of investigations dedicated to hip OA.It is important to note that the hip joint possesses distinct characteristics compared to the other three joints.Therefore, in this systematic review, we wanted to focus on hip osteoarthritis and gave a brief update from the previous studies. This systematic review was conducted in accordance with the Preferred Reporting Items of Systematic Reviews (PRISMA) guidelines. All randomized control trials that compared injection of Platelet-Rich Plasma and Hyaluronic Acid in hip osteoarthritis patients using English languagefrom 2018 until 2023 will be included.Six studies involved in this study with total samples of 237 in PRP group and 220 in HA group. The injection site, injection volume, number of injections, interval, and follow up were varied between these studies. All of the patients are undergoing treatment with ultrasound-guided intraarticular injections of PRP. The outcomes tabulated were Visual Analog Scale (VAS), Harris Hip Score (HHS), and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score which showed improvements from the baseline. All of the studies showed improvement of the score from the baseline.Although, there were improvements, it can be concluded that there was not enough evidence to promote the utilization of intra-articular PRP injections as a treatment for hip osteoarthritis. Since international guidelines only recommend intra-articular steroid injections for managing hip OA, it would be advantageous to conduct additional studies comparing PRP to steroids to assess the effectiveness of PRP injections in treating hip OA.

Keywords:Platelet-Rich Plasma, PRP,Hip, Osteoarthritis, Hyaluronic Acid.

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Introduction

Osteoarthritis (OA) is the most prevalent type of joint disorder in the United States, with over 27 million Americans estimated to be affected. This degenerative condition can impact any joint, primarily targeting the articular cartilage and adjacent tissues. According to a prominent population study based in the US, symptomatic hip OA was observed in 9.2% of adults aged 45 and above, with 27% displaying radiographic evidence of the condition. The prevalence was slightly greater among women. A systematic review of radiographic hip OA prevalence revealed an increase in the average occurrence as age advances for both men and women. Men tend to have a higher incidence of hip OA before the age of 50, whereas women exhibit a higher occurrence thereafter [1].

While there is no definitive cure for OA, various treatment approaches aim to reduce pain, preserve or enhance joint flexibility, and prevent a decline in functionality. Although numerous research studies have explored the application of PRP (Platelet-Rich Plasma) for addressing knee OA, there is a relatively limited number of investigations dedicated to hip OA. The European League against Rheumatism advises keeping hip OA distinct from knee OA due to disparities in anatomy, development, and suitability of treatments [2].

Initially, it is important to note that the hip joint possesses distinct characteristics compared to the other three joints. It has a deeper joint cavity, fewer blood vessels within the cavity, and is susceptible to femoral head necrosis. This can make PRP injection therapy more challenging in the hip, potentially

olimiting the effectiveness of PRP within the hip cavity [3]. Therefore, in this systematic review, we wanted to focus on hip osteoarthritis and gave a brief update from the previous studies.

Method

This systematic review was conducted in accordance with the Preferred Reporting Items of Systematic Reviews (PRISMA) guidelines. Studies were identified through an electronic systematic search of PubMed, Embase (Elsevier), Cochrane Central (Wiley), Scopus (Elsevier), and ClinicalTrials.gov. The search keywords used were related to "osteoarthritis", "hip osteoarthritis", "Platelet-Rich Plasma", "Hyaluronic Acid"using Boolean operator AND and OR. We limited the studies from 2018 until 2023 used in this study to ensure the source was updated and relevant with the current situation. Resulting studies were screened by the relevance of titles and abstracts. We excluded articles that published in non-peer- reviewed journals, lack of an abstract, animal studies, and duplicates of already included papers. All studies that compared injection of Platelet-Rich Plasma and Hyaluronic Acid in hip osteoarthritis patients using English language will be included.We included only randomized control trial (RCT) to maintain the quality of this study.

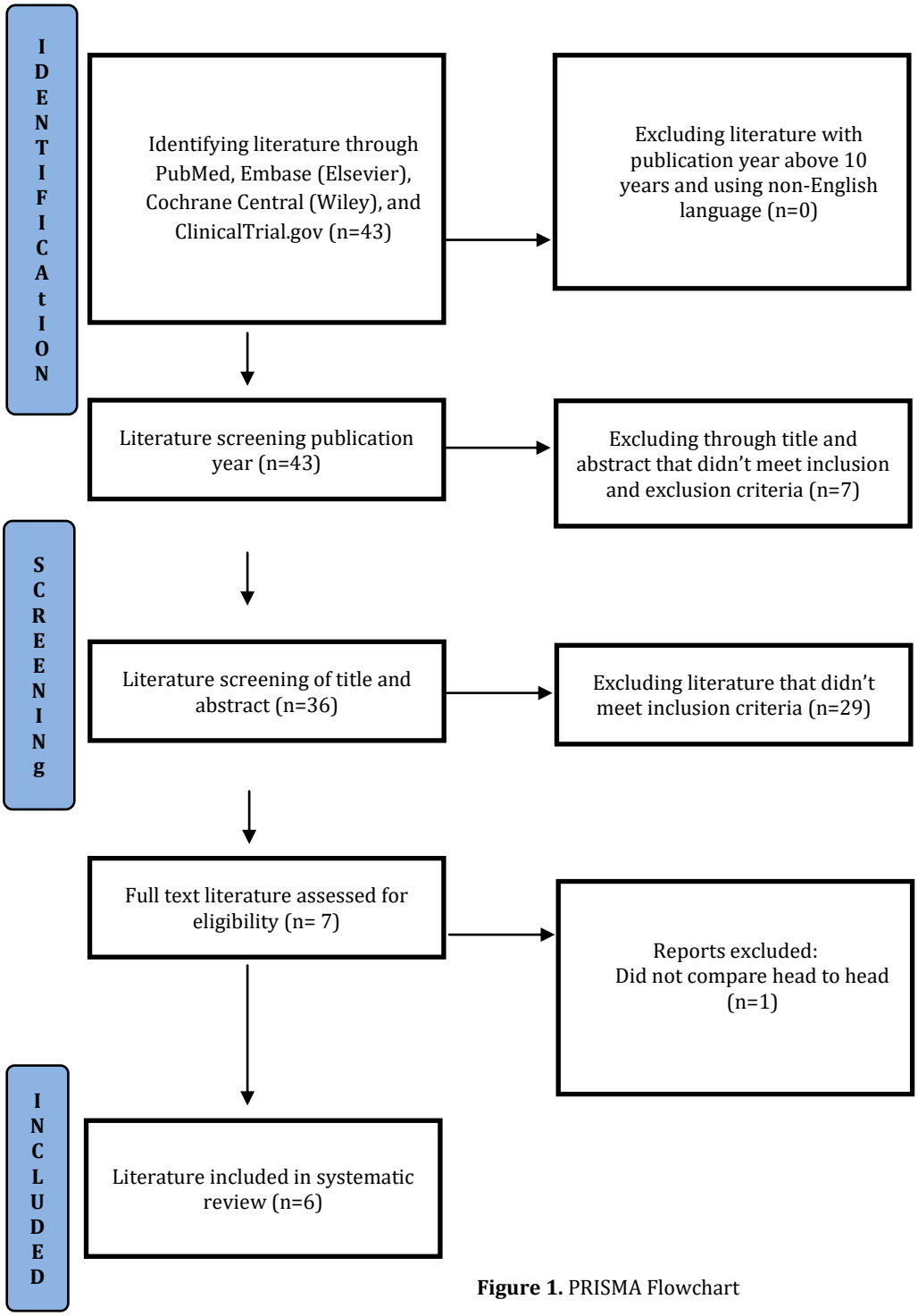

Figure 1. PRISMA Flowchart

Result

There were six studies involved in this study and all of them were RCTs[4–9]. In total, there were 237 samples in PRP group and 220 samples in HA group. The grade of OA was assessed using Kellgren Lawrence grade and varied between these studies (Table 1). The injection site, injection volume, number of injections, interval, and follow up were varied between these studies. All of the patients are undergoing treatment with ultrasound-guided intraarticular injections of PRP which is compared with patients treated with hyaluronic acid. The data has been tabulated in Table 2. The outcomes tabulated were Visual Analog Scale (VAS), Harris Hip Score (HHS), and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score. All of the studies showed improvement of the score from the baseline. Although, this score was not assessed at the same period. Quantitative mean difference was not analysed (Table 3).

Table 1. Tabulated study results

Study	Country	Type of Study	Sample		Age	Hip OA Kellgren Lawrence Grade			
			PRP	HA		I	II	III	IV
Battaglia., et al (2013) [4]	Italy	RCT	50	50	53±12	0	32	42	26
Di Sante., et al (2016) [5]	Italy	RCT	21	22	73±7	Excluded	24	76	Excluded
Dallari., et al (2016) [6]	Italy	RCT	44	36	20-65	31	22	22	25
Doria C., et al (2017) [7]	Italy	RCT	40	40	68±5	N/A	N/A	Excluded	Excluded
Villanova-Lo´pez., et al (2020) [8]	Spain	RCT	38	36	61.2 ± 9.72	14	18	6	
Nouri., et al (2022) [9]	Iran	RCT	44	36	58.22 ± 5.10	Excluded	16	16	Excluded

Table 2. Characteristics of intervention

Study	Injection site	Injection volume (ml)	Number of injections	Injection time	Follow up
Battaglia., et al (2013) [4]	Anterosuperior, parasagittal approach over the base of the femoral neck	5	3	Once per week	Baseline, 1, 3, 6, and 12 months after last injection
Di Sante., et al (2016) [5]	Anterior synovial recess at the junction of the femoral head and neck	3	3	Once per 2 weeks	Baseline, 1 and 4 months after last injection
Dallari., et al (2016) [6]	Anterolateral region of the hip, at the base of the femoral neck	5	3	Once per week	Baseline, 2, 6, and 12 months after last injection
Doria., et al (2017) [7]	Anterosuperior, parasagittal approach over the base of the femoral neck	5	3	Once per week	Baseline, 6 and 12 months after last injection
Villanova-Lo´pez., et al (2020) [8]	Anterolateral approach	6	1	-	Baseline, 1 week, 1 month, and 12 months
Nouri., et al (2022) [9]	Anterior capsular recess, between the neck and head of the femur, in a caudocranial and lateromedial manner	5–6	2	After 2 weeks	Baseline, 2 months, and 6 months

Table 3. Outcomes of studies

Study	Intervention	Outcomes												Adverse Events
		VAS		HHS		WOMAC		WOMAC-Pain		WOMAC-Stiffness		WOMAC-Function		
		Baseline	Post	Baseline	Post	Baseline	Post	Baseline	Post	Baseline	Post	Baseline	Post	
Battaglia., et al (2013) 12 months [4]	PRP	5.47 ± 0.50	4.75 ± 0.67	58.11 ± 3.93	65.73 ± 5.13									one patient developed a superficial hematoma after first infiltration due to transitional venous damage, but spontaneously resolved in 2 week
	HA	5.97 ± 0.49	4.59 ± 0.67	62.90 ± 3.92	72.55 ± 5.13									
Di Sante., et al (2016) [5] 4 months	PRP	7.08 ± 2	6.36 ± 2.10					58.89 ± 22	53.47 ± 22.30	53.72 ± 22.7	47.22 ± 22.70	59.87 ± 22.5	50.80 ± 22.80	-
	HA	6.32 ± 1.70	3.63 ± 2.10					42.36 ± 20.5	19.90 ± 11.40	57.65 ± 26.2	32.91 ± 20.60	45.83 ± 21.7	28.39 ± 17.20	
Dallari., et al (2016) [6] 12 months	PRP	N/A	2.40 ± 0.70			N/A	3.50 ± 0.90							-
	HA	N/A	4.20 ±			N/A	59 ± 0.50							

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			0.80											
Doria., et al (2017) [7] 12 months	PRP	7.50 ± 2.10	6.40 ± 2.90	64 ± 10.30	78 ± 11.30			23.70 ± 2.10	7.40 ± 2.50	3.80 ± 4.10	2 ± 4.20	29.40 ± 2.60	12 ± 3.80	PRP group a significantly higher post-injective pain reaction (p = 0.043).
	HA	7.80 ± 1.90	6.10 ± 2.30	62 ± 9.80	75 ± 11.40			24 ± 1.90	9 ± 5.60	4.30 ± 5.30	3.10 ± 4.30	28.50 ± 2.50	10.90 ± 4.2	
Villanova-Lo´pez., et al (2020) [8] 12 months	PRP	7 [5–8]	5 [1.7-7.3]	51.9 [44.1-64.7]	70.9 [57.2-89]	53.5 [34.5-65.2]	33 [13.7-58]	10 [6.7-14]	7 [1.75-11]	4.5 [2.75-6]	3 [1–4]	36 [24.7-46]	23.5 [13.7-58]	-
	HA	7 [5–8]	6 [2.7-8]	55.8 [48.6-63.5]	60.2 [43-74.2]	50.5 [33.5-60.7]	40.5 [27.2-70.7]	10 [7-13.7]	9.5 [3.75-15]	4 [2-5.7]	3 [1–6]	36 [23-42]	28 [20.2-48.7]	
Nouri F., et al (2022) [9] 6 months	PRP	7.63 ± 1.31	3.13 ± 1.29			41.38 ± 9.36	21.53 ± 10.40	9.53 ± 1.72	4.59 ± 1.83	2.75 ± 1.83	1.03 ± 1.26	29.09 ± 7.09	15.91 ± 7.96	-
	HA	8.10 ± 1.18	3.90 ± 1.40			41.41 ± 11.52	27.21 ± 9.25	9.28 ± 1.41	5.45 ± 1.66	2.38 ± 1.21	1.00 ± 0.96	30.41 ± 8.71	19.93 ± 6.90	

Discussion

One of the therapies that has seen a significant rise in popularity over the last decade is platelet-rich plasma (PRP). PRP is an autologous substance derived from a person's own blood, which has elevated platelet levels and higher concentrations of growth factors, including platelet-derived growth factor (PDGF), transforming growth factor b, and vascular endothelial growth factor [10]. PRP has gained traction as a biological treatment option for managing osteoarthritis (OA). Originally introduced for therapeutic purposes in the late 1980s, PRP has conventionally been known as a plasma volume with an increased platelet count. It is created by centrifuging autologous whole blood, resulting in a blood derivative with a higher platelet concentration than the original sample. PRP has the capability to release cytokines and growth factors at the site of disease after a degranulation process, thereby creating a favorable environment for the healing of soft tissues. This process initially triggers a pro-inflammatory response and subsequently reduces inflammatory molecules. In vitro experiments with chondrocytes treated with PRP have demonstrated stimulation of articular cartilage matrix metabolism, as well as the synthesis of proteoglycans and collagen, resulting in tissue that exhibits histological and biomechanical similarities to the original tissue[11].

In terms of bioactivity, PRP has been reported to contain over 800 proteins, which can lead to various effects, including coagulation and inflammation regulation. Platelets also play a role in delivering active molecules and a wide range of growth factors, which can influence processes like bone or vessel remodeling, inflammation, angiogenesis, collagen synthesis, and cell differentiation. In the context of cartilage effects, TGF-β is believed to support and stimulate chondrocyte synthesis by enhancing cell proliferation and matrix production, as well as promoting bone formation in vivo by working in conjunction with bFGF to induce the migration of specific bone marrow cells[12].

Multiple PRP collection protocols and preparation methods are available through various commercial systems. Typically, the production of PRP involves collecting whole venous blood, which is then mixed with an anticoagulant before undergoing centrifugation. A single or double centrifugation process is used to separate erythrocytes and concentrate platelets. Platelets, often found in the 'buffy coat' along with leukocytes, can be isolated using various methods, either with or without leukocytes. These platelets can be activated with calcium chloride or applied directly without activation [3,13].

PRP can be categorized into different types based on platelet isolation and activation methods, centrifugation speed, and collection systems, and several classification systems exist. One important categorization is based on the leukocyte content, distinguishing between leukocyte-rich and leukocyte-poor PRP, with the former having a higher concentration of leukocytes compared to the baseline. The presence of leukocytes has been associated with increased catabolic cytokines, which may partially counteract the anabolic cytokines found in platelets. Regardless of the preparation method, PRP consistently contains elevated platelets and growth factors and has been demonstrated to have an overall anti-inflammatory effect and a positive impact on chondrogenesis, making it a promising therapeutic intervention for OA [14].

This study was limited by varied characteristic of interventions and limited recent studies. Moreover, only two studies that discussed the adverse event of the interventions. All of the studies showed improvement of the score from the baseline. Although, this score was not assessed at the same period.

Conclusion

Although, there were improvements, it can be concluded that there was not enough evidence to promote the utilization of intra-articular PRP injections as a treatment for hip osteoarthritis. Since international guidelines only recommend intra-articular steroid injections for managing hip OA, it would be advantageous to conduct additional studies comparing PRP to steroids to assess the effectiveness of PRP injections in treating hip OA.

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Conflict of Interest

All authors declare no conflict of interest.

Informed Consent

Written informed consent was obtained from the patient.

Ethical Statement

The patient provided written informed consent for this case to be published.

Author Contribution

RS, FL, and SW designed the study. RS, FL, and SW retrieved the data. RS, FL, and SW analyzed the datadescriptively.RS, FL, and SW wrote the manuscript. All authors approved the final version of the manuscript.

References

1. Lespasio MJ, Sultan AA, Piuzzi NS, Khlopas A, Husni ME, Muschler GF, et al. Hip Osteoarthritis: A Primer. Perm J 2018;22. https://doi.org/10.7812/TPP/17-084.
2. Lim A, Zhu JB, Khanduja V. The Use of Intra-articular Platelet-Rich Plasma as a Therapeutic Intervention for Hip Osteoarthritis: A Systematic Review and Meta-analysis. Am J Sports Med 2023;51:2487–97. https://doi.org/10.1177/03635465221095563.
3. Xiong Y, Gong C, Peng X, Liu X, Su X, Tao X, et al. Efficacy and safety of platelet-rich plasma injections for the treatment of osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Front Med (Lausanne) 2023;10. https://doi.org/10.3389/fmed.2023.1204144.

4. Battaglia M, Guaraldi F, Vannini F, Rossi G, Timoncini A, Buda R, et al. Efficacy of Ultrasound-guided Intra-articular Injections of Platelet-rich Plasma Versus Hyaluronic Acid for Hip Osteoarthritis. Orthopedics 2013;36. https://doi.org/10.3928/01477447-20131120-13.
5. Sante L Di, Villani C, Santilli V, Valeo M, Bologna E, Imparato L, et al. Intra-articular hyaluronic acid vs platelet-rich plasma in the treatment of hip osteoarthritis. Med Ultrason2016;18:463. https://doi.org/10.11152/mu-874.
6. Dallari D, Stagni C, Rani N, Sabbioni G, Pelotti P, Torricelli P, et al. Ultrasound-Guided Injection of Platelet-Rich Plasma and Hyaluronic Acid, Separately and in Combination, for Hip Osteoarthritis. Am J Sports Med 2016;44:664–71. https://doi.org/10.1177/0363546515620383.
7. Doria C, Mosele G, Caggiari G, Puddu L, Ciurlia E. Treatment of Early Hip Osteoarthritis: Ultrasound-Guided Platelet Rich Plasma versus Hyaluronic Acid Injections in a Randomized Clinical Trial. Joints 2017;05:152–5. https://doi.org/10.1055/s-0037-1605584.
8. Villanova-López MM, Núñez-Núñez M, Fernández-Prieto D, González-López C, García-Donaire J, Pérez-Pérez A, et al. Ensayoclínicofase III para evaluar la eficacia y seguridad del uso de plasma ricoenplaquetasfrente a ácidohialurónicoencoxartrosis. Rev Esp Cir OrtopTraumatol2020;64:134–42. https://doi.org/10.1016/j.recot.2019.09.008.
9. Nouri F, Babaee M, Peydayesh P, Esmaily H, Raeissadat SA. Comparison between the effects of ultrasound guided intra-articular injections of platelet-rich plasma (PRP), high molecular weight hyaluronic acid, and their combination in hip osteoarthritis: a randomized clinical trial. BMC MusculoskeletDisord2022;23:856. https://doi.org/10.1186/s12891-022-05787-8.
10. Berney M, McCarroll P, Glynn L, Lenehan B. Platelet-rich plasma injections for hip osteoarthritis: a review of the evidence. Irish Journal of Medical Science (1971 -) 2021;190:1021–5. https://doi.org/10.1007/s11845-020-02388-z.
11. Lim A, Zhu JB, Khanduja V. The Use of Intra-articular Platelet-Rich Plasma as a Therapeutic Intervention for Hip Osteoarthritis: A Systematic Review and Meta-analysis. Am J Sports Med 2023;51:2487–97. https://doi.org/10.1177/03635465221095563.
12. Medina-Porqueres I, Ortega-Castillo M, Muriel-Garcia A. Effectiveness of platelet-rich plasma in the management of hip osteoarthritis: a systematic review and meta-analysis. ClinRheumatol2021;40:53–64. https://doi.org/10.1007/s10067-020-05241-x.
13. Bennell KL, Hunter DJ, Paterson KL. Platelet-Rich Plasma for the Management of Hip and Knee Osteoarthritis. CurrRheumatol Rep 2017;19:24. https://doi.org/10.1007/s11926-017-0652-x.
14. Ye Y, Zhou X, Mao S, Zhang J, Lin B. Platelet rich plasma versus hyaluronic acid in patients with hip osteoarthritis: A meta-analysis of randomized controlled trials. International Journal of Surgery 2018;53:279–87. https://doi.org/10.1016/j.ijsu.2018.03.078.