



### Efficacy of Platelet-Rich-Plasma Injection for Knee Osteoarthritis: A Review Article of Clinical Evidence

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#### Abstract

**Background:** Osteoarthritis (OA) is a chronic and degenerative disease which is mostly seen in adult population. It is common form of joint disability which negatively affect the quality of life of affected people. This study was conducted to review evidence on the use of platelet-rich-plasma (PRP) injection for treatment knee OA, evaluating its efficacy, limitations, and geographical disparities in research.

**Methods:** This review encompassed 39 eligible studies: 11 meta-analyses, 10 RCTs, seven systematic reviews, seven narrative reviews, and four observational studies. It examined key themes such as the comparative efficacy of PRP versus HA, CS, and placebo injection; protocol variability; and long-term outcomes.

**Results:** Applying PRP at early stages and in mid-term (6-12 months) demonstrates significant superiority over HA and steroids in pain reduction and functional improvement, particularly in early-to-moderate OA. However, structural benefits such as cartilage regeneration remain unproven, as well as evidence beyond 24 months is limited. Critical limitations include protocol heterogeneity as leukocyte content, centrifugation methods, statistical fragility in meta-analyses, and publication bias favoring small positive trials. Over 90% of studies originated from high-income countries particularly USA, China, and Europe, while people affected with severe OA and low income countries and regions with constrained resources remained underrepresented.

**Conclusion:** The PRP effectiveness and its feasibility as a second-line therapy for early and moderate cases of knee joint OA confirmed, but its long-term efficacy and cost-effectiveness require further validation. There is a need for conducting RCTs to examine its efficacy after follow-up in longer term ( $\geq 3$  years). Addressing geographical disparities through inclusive research is recommended.

**Key words:** Platelet Rich Plasma, Osteoarthritis, Efficacy, Knee Joint, review article

#### Introduction

Osteoarthritis (OA) is a chronic and degenerative disease which is predominantly seen in adults. Its main symptoms are pain, swelling, crepitus and stiffness of the joint and disturbing the ability of a person to move freely. Osteoarthritis is affecting the entire joint, including its surrounded tissues. OA can affect every joint, but it is most common in the knees, hips, spine and hands joints.

Studies have shown that "the prevalence of Osteoarthritis tends to increase with age and is influenced by underlying risk factors such as gender, obesity, joint injuries

(work/sports activities), and geographic region [1]. Typical characteristics include damage to the joint cartilage and formation of osteophytes (new formed bones at the edge

of bones). These new bone formation is due to metabolic, biochemical, physiological and pathological changes in the joint cartilage and

subchondral bone. Other signs of the disease are asymmetrical swelling and deformity of the joints, as well as inflammation of the joint and changes in gait of patients [2].

Osteoarthritis is affecting negatively the quality of life of affected people. Therefore, it became as a public health problem all over the world.

According to Global Burden of Disease report on 2019; globally about 528 million people were living with osteoarthritis; said report showed an increase of 113% since 1990[3].

According to osteoarthritis year review 2021 report (epidemiology & therapy), more than 22% of adults older than 40 had knee OA, as well as it is estimated that over 500 million individuals are currently affected by OA worldwide [2]. Long H (2022) stated that the knee OA is the most frequently affected joint among people with OA (365 million globally), which is followed by the hip and the hand [4].

In terms of disease severity, considerable number of people living with OA (344 million) experiencing moderate to severe levels whom could benefit from rehabilitation [5].

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At the moment, there are various methods for managing osteoarthritis in terms of reducing pain, applying regeneration and non-regeneration therapy. Non-regeneration therapies include physiotherapy, advising analgesic and anti-inflammatory medicines, applying intra-articular injections such as CS, HA, and geniculate nerve blocks, extra-articular injections and radiofrequency approaches. And, regeneration management consisting laser and intra-articular injection such as prolotherapy and PRP [6].

Day to day increasing rates of injuries and obesities, are expected that the number of people with osteoarthritis will continue to increase internationally.

Among musculoskeletal diseases, osteoarthritis is one of the substantial contributors to quality of life indicators particularly years lived with disability (YLD). Osteoarthritis cases are more prevalent among aged population as 70% cases are reported among people older than 55 years, while most of the time, the disease typical onset is happening in the late 40s to mid-50s. It could also affect younger individuals mainly athletes and those frequently exposed to joint trauma [2].

Number of publications are reported the regenerative and therapeutic benefits of applying PRP injection as a conservative treatment for knee joint osteoarthritis in recent years. There are many controlled trials examined the efficacy of injecting PRP at different stages of osteoarthritis.

Jonathan Dubin et al. at the American Academy of Orthopedic surgeons' technology had conducted a systematic review.

They were reviewed about 54 articles on using Platelet Rich Plasma (PRP) for treatment of knee joint osteoarthritis. They verified the efficacy of using PRP versus injecting CS, placebo/control, NSAIDs, HA, ozone therapy, exercise, prolotherapy, autologous conditioned serum, and bone marrow aspirate concentrate therapy [7].

The effect of PRP intra-articular injection in comparison with other conservative methods for the management of knee joint OA evaluated by Veloso Costa et al (2022). At six months follow-up, they summarized that PRP found effective comparing other treatments in pain, stiffness relief and restored function.

Himanshu Bansal on 2021 conducted a clinical trial with participation of 150 individuals through randomization to receive either PRP (about 10 billion platelets) or HA (4ml for each of 75 patients in each group). After one year follow-up it has found up-to 90% recovery by using improved platelets. Noteworthy progress in WOMAC ( $51.94 \pm 07.35$  versus  $57.33 \pm 08.92$ : P-value less than 0.001), IKDC scores ( $62.8 \pm 6.24$  versus  $52.7 \pm 06.39$ : P-value less than 0.001), six minutes pain free walking distance ( $+120$  versus  $+4$ : P-value less than 0.001) continued in platelet rich plasma in comparison with HA group within one year [8].

The study entitled "PRP and knee OA" [9]. Reported that applying the PRP injection into knee joint will induce a process to help recovery of joint cartilage regenerative capacity. Also its effectiveness in pain relief and joint functional improvement confirmed.

The PRP anti-inflammatory effect through transformation of growth factor- $\beta$  and insulin-like growth factor 1, as well as stimulatory influence on mesenchymal stem cells and fibroblasts is acknowledged by Taylor M Southworth et al. The authors confirmed the PRP superiority to HA and CS in pain and stiffness relief and improvement the scores of functionality. But, they noted many dissimilarities in preparation of PRP. They highlighted lack of standardization in number of factors such as speed and duration of centrifugation, which can lead to extensive concentrations of platelets and leukocytes [10]. The use of PRP in treatment of tendon, ligament, skeletal muscle and knee joint osteoarthritis has been summarized by O'Occunel B

et. al. (2019). He suggested that the efficacy of PRP in treatment of sport associated injuries remaining inconclusive [11]. In Afghanistan, the majority of knee osteoarthritis cases are managing through conservative approaches. In severe cases, specialists advising intra articular injections (corticosteroid, HA). One of the updated treatment of the knee joint osteoarthritis is PRP injection. Review and analysis of previous conducted studies i.e. meta-analysis, systematic reviews, and controlled trials in regards to PRP efficacy and provision of necessary information will help informed decision making process and will guide scientific clinical approaches.

This review aims to evaluate the efficacy of PRP injection in treatment of Knee joint osteoarthritis. Its optimal outcomes at different stages of the disease as well as PRP injection results with other intra-articular injections, such as HA or CS will be identified.

### Material and Method

This narrative review summarizes the current evidence on the efficacy of PRP for the treatment of knee osteoarthritis. To identify relevant literature, a comprehensive search of databases including PubMed, Scopus, EMBASE, and the Cochrane Library was conducted. Google Scholar was used to identify additional grey literature.

The search strategy employed keywords and combinations thereof, including: "platelet-rich plasma," "PRP," "knee osteoarthritis," "treatment," and "efficacy." The search was limited to articles published in English from 2013 to the present (April 2025).

Articles were selected for inclusion based on their focus on the non-surgical use of PRP for knee osteoarthritis. Priority was given to clinical trials, randomized controlled trials, and systematic reviews. Animal studies, studies on inflammatory arthritis (e.g., rheumatoid arthritis), and articles published before 2013 or in languages other than English were excluded.

From an initial pool of 189 identified records, 39 studies were deemed most relevant to the scope of this review. Data from these studies were extracted and summarized narratively to discuss the preparation protocols, efficacy, and outcomes of PRP treatment for knee OA.

### Results

This exercise highlighted applying PRP as a nonsurgical intervention for the treatment of knee joint OA.

In this endeavor, totally 39 studies' reports including 11 meta-analysis, seven systematic reviews, 10 randomized controlled trials (RCTs), seven narrative reviews, and four observational studies reviewed and their key findings regarding PRP Usage in early stages of the disease as its anti-inflammatory and chondro-protective effects found align with slower disease progression. However, applying PRP injection in advanced stages of knee joint osteoarthritis remains contentious due to conflicting evidence on reduction of disease symptoms for longer time and structural benefits.

The evidences showed a critical gap in generalizability. The reviewed articles mostly encompasses high-income regions, as about 78% of studies are originating from the USA, China, and Europe. Low income countries and regions i.e. Africa, and South America contributed less than 5% of publications.

From Methodological aspect, meta-analyses and RCTs were dominated. Key research themes included: relative efficacy (PRP injection versus HA, CS, and placebo injections), inconsistency of protocol (the impact of leukocyte content, activation methods, and injection intervals), and long term data (among reviewed articles, there is no evidence beyond 24-month follow-ups).

**Figure 1** Percentage of studies reviewed.

## Efficacy of

### Platelet-Rich Plasma versus Alternatives

**Symptom Relief:** In this study PRP injection demonstrates statistically significant effect within 6-12 months superiority over HA, CS, and placebo injections in pain reduction (Visual Analogue Score or VAS score) and knee joint functional improvement (WOMAC scores). As, Migliorini reported a 40-50% reduction in pain of those who received PRP injection cohorts comparing to 25-30% reduction with those who received HA injection [12].

**Structural Outcomes:** Notwithstanding reduction in disease symptoms, structural improvements such as cartilage thickness remain elusive. For instance, Bennell (2021) found no significant MRI-based cartilage regeneration in PRP-treated patients. The reports suggesting that its role could be palliative rather than regenerative[ 13].

### Proportional Effectiveness

**Platelet-Rich Plasma versus Hyaluronic Acid:** a meta-analysis conducted by Han Y, et al. in Pain Medicine found that PRP injections were more effective than HA injections for patient with knee joint osteoarthritis, this study revealed superior pain reduction and improved function at 6 and 12-month follow-ups, although HA injection noted more cost-effective in short-term care [ 14].

**Platelet-Rich Plasma versus CS:** study found that the PRP's effects sustained longer than CS. As PRP persisted for More than 12 months, while the corticosteroid effects persisted for 3-6 months. However, the steroid injections develop early faster relief than PRP, as in mid-term evaluation its affect found better than steroid and placebo [15].

### Discussion

This study revealed number of inconsistency in evidences. Different PRP protocols and results measures lead variability. For instance, leukocyte rich PRP might worsen inflammation of joints in sensitive patients. Whereas, leukocyte poor formulation may effect delivery of the growth factor [16].

Statistical significance of PRP in relief of symptoms such as pain, stiffness, and functionality approved [17], while its clinical relevance is contested yet [18]. In

short term less than one year follow-up, PRP intra-articular injection found more effective particularly in relieving pain and joint function improvement than HA and placebo injections. Both types' injections had similar risk of adverse events [19]. But there is an opposite finding that does not support above mentioned progress. The RCT conducted by Bennell KL et al. (2021) suggest that applying PRP injection to individuals with mild and moderate osteoarthritis of the knee joint might not provide a significant benefit over saline to relief pain or decreasing the disease progress [20].

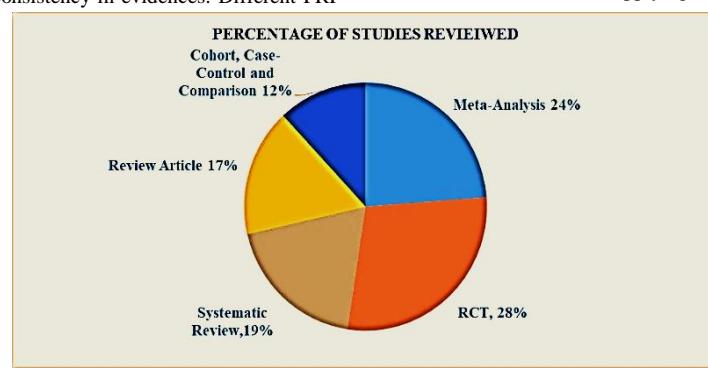
Furthermore, there are some critiques on overlapping in conclusion; O'Connell, (2019) suggest; since the PRP has promised as an alternative for

management of knee joint OA, he recommended further validation for the assumptions [21].

It has revealed that only approximately 60% of patients receiving PRP injections experienced a slight clinical improvement in pain, compared to about 45% of those receiving HA[ 22,23]. However, several studies did not confirm the effectiveness of PRP for older patients or those with severe knee osteoarthritis, instead supporting its use for younger individuals with mild cases [24]. Overall, the review demonstrated a strong favorability for PRP over alternative treatments. Among 30 studies comparing PRP to HA, 25 (83%) favored PRP. Furthermore, 8 out of 15 studies favored PRP over steroid injections. The reported rate of favorability for PRP across all comparisons ranged from 53% to 92%.

The majority of studies reviewed in this endeavor, favoring applying PRP for treatment of knee joint OA. Nonetheless, none of them discussed its feasibility in poor settings and low income countries. As well as some RCTs are conducted with small number of sample size (Bizacchi, 2018) or with limited generalizability [25,26]. This review discovered some limitations; variability founded in PRP preparation, as single versus double centrifugation, as well as leukocyte-rich versus leukocyte-poor PRP, lead to misperceive outcomes. Leukocyte-rich PRP might induce transient synovitis, divert assessment of pain relief [27,28].

The studies reports which are published internationally, showed publication bias as there are overrepresentation of positive outcomes in industry-funded studies. While there is less than 5% evidences from low income countries. This study showed that about 90% of RCTs reviewed were conducted in high-income countries, consequently there remain limited intuitions on applying PRP injections' feasibility in low and middle income countries, or the studies reported from a single center [29]. As well as the patients who are sever stages of osteoarthritis constitute less than 10% of study cohorts. From ethical perspective, applying PRP's associated with high cost and lack of insurance coverage in many countries lead to worsening healthcare inequities, particularly in places where HA or corticosteroid injections are more feasible.



### Conclusion

PRP injection found a feasible second-line therapy for treatment of knee joint osteoarthritis at early to moderate stages of the disease. Its efficacy confirmed within 6-12 months. However, PRP efficacy in long run beyond 24 months is not yet proven. The study findings highlighted inconsistency in protocols which hamper its clinical use, as thresholds of leukocyte content and platelet concentration need consensus. Though, the PRP's benefits over HA and CS at early and mid-stages of the osteoarthritis confirmed, but its cost in low income countries with limited resources not justified.

### Recommendations

Evidences of current review shows that there is need for development of an international guidelines for centrifugation methods, platelet counts, and leukocyte stratification. Categorizing of PRP types, for instance intra articular leukocyte-poor PRP (LP-PRP) and leukocyte-rich PRP (LR-PRP) in trial reporting is required. In order to evaluate the PRP effectiveness in

longer period, there is need for conducting RCTs with three or more than three years follow-up with imaging and efficiency metrics. Since there are no evidences from poor resources settings, building partnership to conduct trials in South Asia and African countries will be helpful.

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