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Advancements In Osteoarthritis Management Through Platelet-Rich Plasma Applications

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Abstract: Osteoarthritis (OA) is a common problem. It causes pain and makes it hard to move. Platelet-rich plasma (PRP) injections could be a treatment option. However, how well they work is unclear. We also need to know more about their safety compared to standard treatments. This review looks at how well PRP injections work for OA. We also examine their safety by studying data from clinical trials. We included studies if they tested PRP injections for hip OA. The studies also had to report any bad effects. All studies showed that PRP reduced pain and improved movement. There was no major safety issues reported. This suggests PRP is safe. Minor side effects were short-lived and went away on their own. The quality of the studies varied from low to high. In conclusion, PRP injections seem safe and effective for OA. They appear to work better than hyaluronic acid. More research is needed to make PRP treatments standard. We also need to study the long-term safety and effects.

Keywords: intra articular injection, osteoarthritis , orthobiologic, platelet-rich plasma.

I. Introduction

Osteoarthritis (OA) is a long-term joint problem. It involves cartilage breaking down and bone changes. It is a main cause of pain and disability in adults. This problem affects their lives and costs healthcare systems a lot of money, according to Bourne et al. and Cross et al. [1,2]. Hip OA involves stress, chemicals, and genes. These cause joint damage and swelling [3].Normal treatments for hip OA aim to ease pain and improve movement. These include exercise, pain medicine, and injections [4]. These treatments can help with symptoms. However, they often do not fix the cause and can have side effects [5]. For severe cases, surgery like hip replacement might be needed. Still, surgery has risks and requires recovery.

Recently, regenerative medicine has become popular for joint problems. Platelet-rich plasma (PRP) injections are getting more attention. PRP is prepared from a person's own blood. It has a high amount of growth factors. These factors may help repair tissue and reduce swelling [6]. PRP could help the body heal itself. This may slow down the disease and improve results. PRP therapy has promising ideas behind it. However, results for hip OA are mixed. It is not always clear if it eases symptoms and improves joint function. Other treatments like hyaluronic acid (HA) injections exist. Some studies have looked at these results, including reviews by Medina-Porqueres et al. and Veronesi et al. [7,8]. Medina-Porqueres et al. [7] looked at four trials. These compared HA to PRP for pain and movement. Two trials found no difference between the groups.

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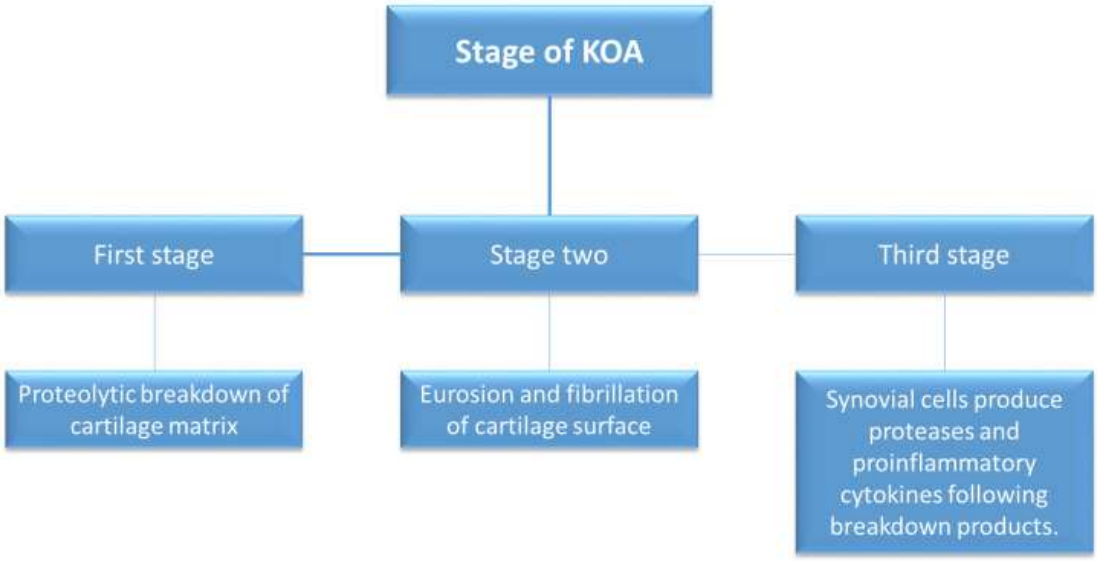
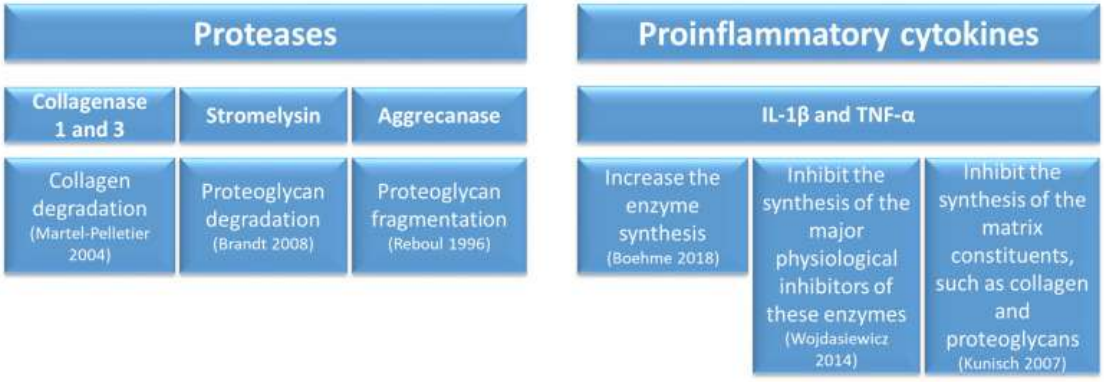
Figure 1



KOA's third stage involves several changes. Collagen and proteoglycan break down at this point. Pro-inflammatory enzymes increase, causing problems. The body struggles to make matrix parts [9 -15].

Figure 2 shows this process.



Third-stage KOA involves multiple pathways [9-15]. Age significantly impacts osteoarthritis (OA). It affects cartilage's extracellular matrix [16]. OA causes degeneration in joints. Articular cartilage, bone, and connective tissue are affected. The joint's metabolism also becomes abnormal [17,18]. OA is marked by structural and molecular changes [19]. Cartilage erosion and tissue loss are frequent. Sub-chondral bone cysts and osteophytes often form [20]. Knee OA causes pain, stiffness, and disability. Swelling and loss of function also occur. Diagnosis uses radiography, MRI, or CT scans [21].

Cartilage and chondrocyte issues are key in KOA knees. Cartilage erodes with tissue loss. Hyaline cartilage gathers water. Proteoglycan levels decrease, reducing cartilage stiffness. Subchondral bone cysts and osteophytes are typical(20). Main knee osteoarthritis symptoms are pain and stiffness. Disability, loss of function, and swelling are also present. Knee radiography, MRI, or CT scans confirm the diagnosis[21]. Younger patients often suffer ligament and meniscus injuries. This increases the risk of OA later in life [22,23]. These injuries aren't always from trauma. This suggests a link to OA development [24-26]. Preventing and delaying OA is essential, especially in younger people [37].

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1. Pharmacological Treatment of Knee Osteoarthritis

KOA pathology often needs a long-term approach. Short-term treatments are often prioritised [28,29]. Lifestyle changes and weight loss are cost-effective. However, these patient-controlled measures are overlooked [30,31]. Initial KOA treatment focuses on symptom relief [32]. Non-drug and drug methods are used. These may only give short-term relief [43]. Corticosteroid injections might worsen symptoms. They can cause cartilage degeneration [34,35].

1.1. Platelet Rich Plasma

Platelets, also called thrombocytes, come from bone marrow. They are small, discoid cells, about 2 µm wide. Healthy individuals have 150,000 to 400,000 platelets per ml [37-39]. Platelets mainly cause aggregation. They help stop bleeding through adhesion, activation, and aggregation. Vascular injuries activate platelets. They release factors for coagulation from secretory granules. Each platelet holds about 50–80 granules. These include dense granules, o-granules, and lysosomes [39].Platelets were once seen only as hemostatic agents. Now, research shows they affect inflammation. They also impact stem cell migration, proliferation, and angiogenesis. This is due to their growth factors and cytokines [40].When PRP platelets activate, P-granules degranulate. This releases growth factors and cytokines into the surrounding area. PRP treatments rely on these emitted growth factors. In platelet-rich plasma (PRP) use, several growth factors are key. These include vascular endothelial growth factor and transforming growth factor beta (TGF-β1). Also important are platelet-derived epidermal growth factor (PDEGF), insulin-like growth factor (IGF), and basic fibroblast growth factor (b-FGF or FGF-2). Table 1 highlights specific traits of each factor [22]. Their shared ability to stimulate angiogenesis is of great interest [38,41,42].

Table 1. Most-studied growth factors and specific traits.

Function	Growth Factors	Ref.
• Activates the production of KGF. • Regulates angiogenesis and wound contraction. • Promotes collagen synthesis, matrix and epithelialization. • Is responsible for the growth and differentiation of fibroblasts, myoblasts, osteoblasts, nerve cells, endothelial cells, keratinocytes and chondrocytes. • Acts as a mitogen for mesenchymal stem cells. • Stimulates the proliferation of myoblasts.	basic Fibroblast growth Factor(b-FGF)	[43- 48]
• Induces neovascularization by promoting proliferation and migration of macrovascular endothelial cells. • Promotes angiogenesis and participates in the formation of blood vessel lumen indirectly through the release of nitric oxide.	Vascular Endothelial Growth Factor (VEGF/VEP)	[43,44 ,45 ,46 ,47 ,49]

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Function	Growth Factors	Ref.
• Initiates the regeneration of blood circulation and supports wound healing. • Activates the synthesis of metalloproteinase and is involved in the degradation of interstitial collagen types 1, 2 and 3. • Stimulates the chemotaxis of macrophages and neutrophils.		
• Stimulates endothelial angiogenesis. • Regulates the secretion of collagenase. • Stimulates epithelial and mesenchymal mitogenesis. • Supports wound healing by stimulating the proliferation of keratinocytes and dermal fibroblasts.	Platelet-Derived Epidermal Growth Factor (PDEGF)	[44,45 ,46 ,49]
• Stimulates endothelial chemotaxis and angiogenesis. • Participates in the regulation of the balance between fibrosis and myocyte regeneration. • Inhibits the formation of osteoclasts and bone resorption. • Promotes chondrocyte proliferation and extracellular matrix synthesis, essential for cartilage repair. • Inhibits the proliferation of macrophages and lymphocytes. • Stimulates the chemotaxis of fibroblasts. • Increases the synthesis of type I collagen and fibronectin and regulates the secretion of collagenase. • Stimulates or inhibits endothelial, fibroblastic and osteoblastic mitogenesis. • Inhibits DNA synthesis in human fibroblasts.	Transformative Growth Factor Beta (TGF-β1)	[43,44,46,47,49 ,50]

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Function	Growth Factors	Ref.
• Regulates the mitogenic action of other growth factors.		
• Stimulates the growth of myoblasts and fibroblasts. • Activates the synthesis of collagenase and prostaglandinE2infibroblasts. • Regulates the metabolism of articular cartilage through increased synthesis of collagen and matrix osteon. • Stimulates cartilage growth, bone matrix formation and replication of preosteoblasts and osteoblasts. • Together with PDGF, it can increase the speed and quality of wound healing by activating collagen synthesis. • Mediates the growth and repair of skeletal muscles.	Insulin-like Growth Factor (IGF)	[44,45,46,47,48,49]

1.2. Platelet Rich Plasma Preparation

Platelet-rich plasma (PRP) is made using differential centrifugation. It can be prepared in two ways. The open method risks contamination (48,49,50). The closed method uses anticoagulants (51). Centrifugation creates three layers. There is debate about adding leukocytes to PRP (52,53,54). Activation is also debated. Substances like calcium gluconate can start clotting for local effects (55,56).The best PRP concentration is debated. Current devices reach 2–5 times baseline levels. Levels above 2.5 times might hinder the desired action (57-59). Growth factors released after use can last a year. Multiple administrations are needed due to platelet half-life (53).Studies explore carriers such as gelatin hydrogel and hydroxyapatite. Chitosan PRP hybrids are also being investigated. These may improve growth factor efficiency and extend effects. Animal tests show promise (60,61)

2. Benefits of PRP Treatment in Knee Pathology

Orthopaedic and sports medicine are very interested in PRP. It can treat ligament, tendon, and bone lesions (62). Growth factors from PRP help cell recruitment, angiogenesis, and proliferation. This reduces inflammatory enzymes (62,63).PRP can improve the metabolic functions of injured structures. It transmits a regenerative signal. This could affect stem cell proliferation and chondrogenesis (50,64,65).Platelet growth factors help cartilage proliferation. When applied to chondrocytes, they aid protein transcription and cell growth. They also help with cell migration and matrix synthesis. They signal tissue healing and control inflammation (66). In joints with osteoarthritis, PRP affects local and infiltrating cells. It also affects synovial and endothelial cells plus cartilage and bone cells (67). It may slow joint disease by reducing inflammation and angiogenesis. It can also decrease cartilage breakdown and increase anabolism (40).

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PRP might be a primary analgesic treatment. It can speed up the proliferation of tenocytes, osteoblasts, and mesenchymal stem cells (68,69). By involving the whole joint complex, PRP injections can improve clinical outcomes. They may provide short-term remission of osteoarthritis symptoms. It may even delay the need for knee arthroplasty (70). Results are not final, but PRP treatments are better than hyaluronic acid or a placebo for all stages of knee osteoarthritis (71). Compared to HA injections, PRP offers more benefits for treating OA. These include better joint function and better long-term symptom relief. Patients have better outcomes at 3, 6, and 12 months compared to placebo, steroids, or HA injections (72,73,74). WOMAC scores (Figure 3) are also lower (better) with PRP compared to HA or corticosteroid treatment (75).Studies mostly favour PRP treatment. It is generally safe and provides good results. However, it has some disadvantages.

Table 2.(32) Advantages and disadvantages of PRP treatment in the most recent studies.

Criteria	**Benefits**	**Challenges**	**Other Considerations**	**Ref.**
Minimal Invasiveness	✓	✓	Does not involve any surgery, incisions or healing	[73]
Rapid Preparation	✓	-	Does not require any preservative	[73]
Compatibility with Patient Cells	✓	-	Use of patient cells without any further modification	[74]
Comprehensive Therapeutic Effects	✓	-	Can simultaneously reduce synovial inflammation, protect cartilage and reduce pain	[75]
Contaminant Reduction	✓	-	Minimization of blood-borne contaminants	[74]
Accelerated Recovery Time	✓	-	Recovery period reduced	[73]
Enhanced Biocompatibility	✓	-	Does not elicit an immune response	[73]
Morbidity at Injection Site	-	✓	Disadvantage only at the local level	[75]
Standardization of Methods	-	✓	Does not exist	[75]

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Criteria	Benefits	Challenges	Other Considerations	Ref.
Scar Tissue and Calcification	-	✓	Local risk	[74]
Optimal Processing and Concentration	-	✓	Incompletely elucidated	[74]
Risk of Infections	-	✓	Disadvantage only at the local level	[75]
Risk of Allergic Reactions	-	✓	Disadvantage only at the local level	[73]
Unknown Frequency and Volume	-	✓	Does not exist	[74]
Contraindications for Certain Conditions	-	✓	Incompletely known	[75]

✓ = presence of benefits/challenges, - = absence of benefits/challenges

Jang et al. reviewed 65 osteoarthritis patients who had a single PRP injection in their knee. Most felt better after six months, but the effect faded after a year [76]. Torrero et al. studied 30 patients with mild knee damage. They saw positive results six months after a single PRP injection [77].Hart et al. gave nine PRP injections to 51 patients over a year. These patients had mild cartilage damage and showed marked improvement [78]. Patel et al. conducted a trial on 78 patients (156 knees) with osteoarthritis in both knees. The patients who received PRP injections fared better than those who had saline injections. A single dose of PRP with filtered white blood cells worked as well as two PRP injections [79].Filardo et al. compared two ways of preparing PRP in 144 patients with osteoarthritis. Both groups improved after one year. The single-spin method led to less pain and swelling [70].Bansal et al. studied 150 patients over three years. Half received PRP, and half received HA. Both groups improved after one month. The PRP group still felt the benefit after a year, but the HA group declined after that (3, 6, 9 and 12 months) [58].

3.Efficacy

PRP injections often reduced pain for up to 12 months [80-83]. However, one study saw pain relief that was short-lived [81]. It did not last at the 16-week follow-up. Clinical trials used WOMAC to measure functional improvement [80-84]. Most trials showed functional improvement with PRP injections [80,82,83]. Yet, one study saw no significant functional improvement [81]. In that study, functional improvement was lost after 12 months. HA injections also helped manage hip OA. Patients reported less pain and better function [80-84]. Still, PRP worked better for pain reduction [81]. It also improved function more effectively [82]. Combining PRP and HA was not better than PRP alone [81,82]. PRP may be enough for effective management.

4. Safety

PRP and HA both showed good safety. No major problems were reported in any study. Minor side effects were brief. These included local pain or discomfort. They went away without more treatment [80-84]. PRP injections may cause more local symptoms than HA alone [83].

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5. Safety Comparison

One study with 74 patients found no bad effects from PRP or HA [80]. This shows PRP injections are safe. Another study with 43 patients also found no problems [84]. This supports the safety of both treatments. A study with 111 people reported no serious issues with PRP injections [81]. This adds to the evidence of their safety. In a study of 105 patients, 17 had minor side effects [82]. These included pain, warmth, and stiffness. The PRP groups had more pain than the HA group (P-value 0.001). But, overall safety was still high. A study with 80 patients noted more pain after PRP injections (P-value 0.043) [83]. However, there were no major problems.

5.1. Overall summary

PRP injections were well-tolerated across five studies. Few adverse events were reported. Neither PRP nor HA had major complications. This reinforces PRP's safety as a treatment.

6. Future Research Directions

We need to standardise PRP preparation and use. This will allow better comparisons between studies. We also need to find patient traits that predict how they will respond to PRP or HA. This could improve treatment. Longer studies should check how long PRP benefits last. They should also explore PRP's role in hip OA management.

II. Conclusions

These studies suggest PRP is a good option for hip OA. It shows promise in both how well it works and how safe it is. HA helps with pain, but PRP could be better. This is true for people who do not get better with normal care. Trials show PRP can help patients feel much better. Plus, it is a safe way to get treatment. More study is needed on PRP. Future work should create standard rules for PRP use. Also, its long-term safety should be checked in many kinds of patients.

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Figure 3 WOMAC scores

Severity, on average, during the last 48 hours, of:

Pain

	None	Slight	Moderate	Severe	Extreme
Pain – Walking	☐	☐	☐	☐	☐
Pain – Stair climbing	☐	☐	☐	☐	☐
Pain – Nocturnal	☐	☐	☐	☐	☐
Pain – Rest	☐	☐	☐	☐	☐
Pain – Weightbearing	☐	☐	☐	☐	☐

Stiffness:

Morning Stiffness	☐	☐	☐	☐	☐
Stiffness occuring during the day	☐	☐	☐	☐	☐

Level of difficulty performing the following functions, on average, during the last 48 hours:

	None	Slight	Moderate	Severe	Extreme
Descending stairs	☐	☐	☐	☐	☐
Ascending stairs	☐	☐	☐	☐	☐
Rising from sitting	☐	☐	☐	☐	☐
Standing	☐	☐	☐	☐	☐
Bending to the floor	☐	☐	☐	☐	☐
Walking on flat	☐	☐	☐	☐	☐
Getting in/out of a car	☐	☐	☐	☐	☐
Going shopping	☐	☐	☐	☐	☐
Putting on socks	☐	☐	☐	☐	☐
Rising from bed	☐	☐	☐	☐	☐
Taking of socks	☐	☐	☐	☐	☐
Lying in bed	☐	☐	☐	☐	☐
Getting in/out of bath	☐	☐	☐	☐	☐
Sitting	☐	☐	☐	☐	☐
Getting on/off toilet	☐	☐	☐	☐	☐
Performing heavy domestic duties	☐	☐	☐	☐	☐
Performing light domestic duties	☐	☐	☐	☐	☐

The WOMAC parameters are:
0 – none, 1 – slight, 2 – moderate, 3 – severe, 4 – extreme.
The index is out of a total of 96 possible points, with 0 being the best and 96 being the worst

Conflict of Interest

All authors declare no conflicts of interest.

Author Contribution

Authors have equally participated and shared every item of the work.

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