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Platelet-rich plasma in the treatment of osteoarthritis – a systematic review

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Abstract

Introduction: Platelet-rich plasma (PRP) is an autologous preparation gaining popularity in regenerative medicine. It is prepared from a patient's blood by centrifugation, which results in a much higher concentration of platelets than in a standard sample. The rich content of growth factors and signaling molecules provides proliferative and regenerative effects on other cells. These properties are generating considerable interest in plasma for the treatment of degenerative diseases.

Purpose: This systematic review analyzes the evidence from different studies evaluating the validity of platelet-rich plasma in the treatment of degenerative diseases.

Materials and Methods: The article was written based on scientific papers available on PubMed and Google Scholar.

Results: Platelet-rich plasma has demonstrated beneficial effects on joint health in patients with osteoarthritis (OA). Most studies report pain reduction and improved joint function following PRP treatment. When combined with other agents, such as hyaluronic acid, PRP may have synergistic effects. The most favorable outcomes are observed in younger patients with early-stage OA.

Conclusions: PRP injections may represent a significant component of osteoarthritis (OA) treatment. However, this approach requires standardization in terms of preparation methods, concentration of individual components, as well as the volume and frequency of administration.

Keywords: osteoarthritis, platelet-rich plasma, cartilage, intra-articular treatment, hyaluronic acid, LP-PRP, LR-PRP

Introduction

Osteoarthritis (OA) is a serious problem of the world's aging population and the most common cause of musculoskeletal disorders. OA affects not only cartilage but all tissues that make up the joint. The pathogenesis is not fully understood, but the influence of risk factors such as age, obesity, and overuse is well established[1]. Despite the high prevalence and persistence of symptoms, no effective disease-modifying treatment currently exists. Available therapies are limited to symptom management and are often associated with side effects. Researchers are actively investigating new strategies to alleviate pain and slow disease progression. [2,3,4] .

There is great interest in the use of platelet-rich plasma, which has been used successfully in other areas of medicine, such as gynecology, dentistry and dermatology.[5,6,7] The presence of many growth factors and cytokines makes PRP a fundamental substance in regenerative medicine. Another advantage is the safety of autologous plasma. However, studies on the clinical use of PRP have produced inconsistent results, largely due to variations in preparation protocols and the resulting differences in PRP composition[8],[10]. Nevertheless, most studies indicate that properly standardized PRP can relieve pain and promote joint tissue regeneration, particularly when used in combination with other treatment modalities [9,11,12].

Pathogenesis of OA

What we know for sure about OA is that it results from joint overloading and subsequent damage to the articular cartilage. The disease affects the entire joint, causing sclerosis of the subchondral bone tissue, formation of degenerative cysts, excessive synovial exudate, and thickening of the joint capsule and ligaments.

Due to the clinical importance of the problem, researchers aim to elucidate the molecular mechanisms in detail to facilitate the development of effective therapies. Inflammatory processes in the affected joint are driven by various cytokines released from monocytes and macrophages. Moreover, the local joint microenvironment exhibits a disrupted balance between catabolic and anabolic processes, with a predominant shift toward catabolism. Matrix metalloproteinases (MMPs), activated in response to the inflammation, play a key role in this catabolic dominance [13]. Blocking any of the steps in this cascade of joint degradation could result in blocking the progression of the disease.

Treatment of OA

The severity of osteoarthritis as a public health issue is exacerbated by the lack of adequate treatment options. The mainstay of treatment is analgesic therapy, primarily with non-steroidal anti-inflammatory drugs (NSAIDs), which, when used chronically, are associated with numerous side effects, including gastric and duodenal ulcers, dyspepsia, and bleeding. At the same time, NSAIDs help reduce inflammation within the joint.

Another symptom-reducing drug is duloxetine - serotonin-norepinephrine reuptake inhibitor (SNRI) that modulates pain perception by enhancing descending inhibitory pathways in the central nervous system. In osteoarthritis, it helps reduce chronic pain, especially in patients with a neuropathic or centrally mediated pain component. However patients are often dissatisfied with the treatment outcomes or concerned about gastrointestinal side effects, leading them to discontinue regular use.

Physical therapy, appropriately selected exercise, and weight loss slow the progression of the disease, but patients' cooperation in this area is extremely poor[14,15,17]. They do not feel immediate relief, so they question the effectiveness of these methods. Intervention in this area often occurs too late, at which point even minimal physical activity becomes too difficult and painful to perform.

The last resort in osteoarthritis is arthroplasty. It provides unquestionable pain relief and improved functionality[18] but it involves major surgery and long-term rehabilitation. This surgery is mainly required by older people with multiple burdens, which increases the risk of complications.

Recently, the use of intra-articular therapeutic agents has become widespread. Corticosteroids, for example, are widely used in orthopedics; however, their efficacy in the treatment of osteoarthritis remains limited [16]. Hyaluronic acid provides better results. It is a component of synovial tissue, improves the properties of synovial fluid, reduces inflammation[20] and has been shown in some studies to have a positive effect on pain receptors[19]. Recently, there have been an increasing number of studies on the injection of adipose-derived stem cells[36]. Very good results in slowing osteoarthritis and reducing pain have been achieved by administering platelet rich plasma[21].

Characteristics of PRP

Platelet-rich plasma (PRP) is obtained by centrifuging the patient's own blood in specialized tubes. The autologous origin of the preparation ensures a high level of safety and low immunogenicity. A critical factor in the separation of blood components is the selection of appropriate centrifugation speed and duration, as these parameters influence the concentration of other blood cells in the final product.

This is an important aspect, as a 2014 in vitro study by Braun et al. demonstrated that plasma with a high leukocyte content (LR-PRP) has a detrimental effect on joint tissue, leading to synoviocyte death and increased inflammatory markers. In contrast, LP-PRP, plasma with a low leukocyte content, supports extracellular matrix repair and slows cartilage degeneration[22].

PRP owes its unique regenerative effect to the presence of multiple growth factors. Centrifugation results in a small volume of fluid with a very high concentration of platelets, much higher than in blood. Each platelet contains granules filled with numerous growth factors. The most important of these are TGF-β1, PDGF, IGF-1 and VEGF, which, after platelet activation, are responsible for repair processes: they stimulate the proliferation of mesenchymal cells, fibroblasts, angiogenesis and extracellular matrix production[23]. Among the key functions of cytokines present in PRP is their anti-inflammatory effect, which is mediated in part by hepatocyte growth factor (HGF) and tumor necrosis factor-α (TNF-α), both of which interfere with NF-κB transactivation [24]. LP-PRP has a stronger anti-inflammatory effect than LR-PRP[25].

Another issue that needs standardization is the number and volume of injections that give the best results in treating degeneration. There are studies showing that three and five doses of PRP produce significantly better results than a single administration[26,27]. However, there is no established best preparation and dosage regimen for PRP. This makes it difficult to compare different studies and to draw definitive conclusions about the effectiveness of plasma.

This problem was noted by Milants et al. who analyzed 11 studies of PRP injections prepared in different ways[40]. They compared centrifugation method, volume, presence of leukocytes, and number of injections. The authors suggest that the best results are achieved after a single centrifugation of the sample and its preparation to ensure it is free from leukocytes . The optimal thrombocyte concentration was defined as not exceeding 5 times the baseline value. If these results were analyzed in a larger number of subjects and established as a standard, it would allow a better comparison of the performance of PRP with other substances.

Growth factor	Full name	Function
TGF-β1	Transforming growth factor -β1	Supports the production of extracellular matrix and stimulates mesenchymal cell proliferation, supports angiogenesis
PDGF	Platelet-derived growth factor	Stimulates fibroblast division and chemotaxis, collagen production
IGF-1	Insulin-like growth factor	Strongly stimulates tissue proliferation and regeneration
VEGF	Vasculogenic growth factor	Stimulates angiogenesis, increases vascular permeability to blood cells
FGF	Fibroblast growth factor	Modulates collagen organization and stimulates angiogenesis, supports chondrocyte growth and differentiation
EGF	Epidermal growth factor	Supports cell proliferation
HGF	Hepatocyte growth factor	Stimulates cell proliferation, inhibits apoptosis, anti-inflammatory
TNF-α	Tumour necrosis factor	Regulation of inflammatory response and apoptosis

Table 1. Growth factors contained in platelet granules and their functions.

Study Results

A 2024 randomized clinical trial by Yoshioka et al. evaluated the efficacy of autologous leukocyte-poor platelet-rich plasma (LP-PRP) in patients with knee osteoarthritis[28]. The study included 30 participants, with 15 receiving three intra-articular injections of LP-PRP and 15 receiving placebo injections. Clinical outcomes were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Visual Analog Scale (VAS) for pain.

At the 24-week follow-up, the PRP group showed a mean improvement of 75.9% on the WOMAC scale, compared to 27.7% in the placebo group. Additionally, 73.3% of participants in the PRP group reported at least a 50% reduction in pain, as opposed to 28.6% in the placebo group. These findings suggest that LP-PRP is significantly more effective than placebo in improving symptoms and reducing pain in patients with knee osteoarthritis. However, it is important to note the small sample size of the study.

A slightly larger number of 150 subjects was collected in another study conducted in the same year by Qiao et al[29] . In this case, the focus was on evaluating biomarkers of inflammation (IL-1β, TNF-α, hs-CRP). Changes in joint function were determined by the Lysholm and Fugl-Meyer scales. The effect of PRP was compared with etocoxib (NSAID). The number of PRP injections was relatively high, as they were administered every two weeks over a six-month period.

However, the results were compared only after first and second month of treatment, which showed that the success rate of PRP was 94.67% compared to 84% obtained with etoricoxib. Unfortunately, the effects of treatment after 6 months were not studied. The results suggest that platelet-rich plasma has a stronger anti-inflammatory effect than the NSAID drug.

One of the most commonly used analgesics for osteoarthritis is acetaminophen. A 2016 study compared its effects with LP-PRP[37]. The trial lasted 24 weeks and included 65 patients with 1-2 degrees of knee osteoarthritis. Thirty-two patients took 500 milligrams of acetaminophen 3 times a day for 6 weeks, and the remaining patients received 3 injections of LP-PRP every 2 weeks. At baseline, the average VAS pain score was 5.9 in the acetaminophen group and 4.9 in the PRP group. After 12 weeks, pain scores decreased to 1.9 in the PRP group and 4.1 in the oral treatment group. WOMAC scores also showed a significant reduction in both groups, with the PRP-treated group scoring nearly twice as low as the group treated with acetaminophen.

Despite suggestions that leukocyte-rich PRP (LR-PRP) may be less effective than leukocyte-poor PRP (LP-PRP) for treating arthritic joints, LR-PRP has still demonstrated superior outcomes compared to hyaluronic acid (HA) in clinical studies. In a 2021 randomized controlled trial by Park et al., 110 patients with knee osteoarthritis received a single injection of either LR-PRP or HA[30]. After six months, the PRP group showed a significantly greater improvement in function, with an average increase of 11.5 points in the International Knee Documentation Committee (IKDC) score, compared to a 6.3-point increase in the HA group. A previously mentioned in vitro study[22] suggests the advantage of plasma with lower leukocyte content, but in human clinical trials the results are inconclusive.

The 2012 study by Filardo et al.[38] included 144 patients. The authors compared the effects of plasma obtained by single and double centrifugation. 72 subjects received a preparation obtained by single centrifugation without leukocytes (PRGF) and the rest were treated with a preparation with high concentrations of white blood cells (PRP) obtained by double centrifugation. Both methods resulted in similar improvements in IKDC, VAS and Tagner scale, but neither preparation was significantly more effective. It should be noted that the preparation of LR-PRP (PRP) involved freezing 2 of the 3 samples administered to each patient, whereas LP-PRP (PRGF) was always prepared immediately before injection. Perhaps the low temperature storage affected the leukocyte activity.

Regardless of the composition of the PRP, the researchers found that significantly better results were achieved in younger patients with less advanced degenerative disease.

Confirmation of this thesis can be found in a randomized controlled trial conducted in 2013 by Jang et al. They compared the results of a single injection of PRP in patients with Kellgren-Lawrence grade I, II, and III osteoarthritis. The KL I group achieved a reduction in pain from 7.3 to 3.3 on the VAS scale at 6 months, an effect that lasted up to 9.9 months. In contrast, in the KL III group, VAS decreased from 7.7 to 5.3 at 3 months and 6.1 at 6 months, and the effect lasted 5.6 months. Similar results were obtained when comparing the IKDC scale scores in the study groups. In patients with mild osteoarthritis, PRP not only worked better but also lasted longer.

PRP in combination with other substances

A randomized controlled trial conducted on 174 patients with knee osteoarthritis by Fossati et al. (2024) is a paper worth analyzing[31]. The researchers tested the synergistic effect of PRP with hyaluronic acid and compared it with the results obtained when they were used separately. The duration of the experiment was 12 months, and the effectiveness of the therapy was evaluated using WOMAC scales. In the end, all groups showed improvement after 3, 6 and 12 months, but there were no statistically significant differences between them. According to this study, both substances have similar beneficial effects on degeneration, whether given separately or together.

A similar study, but on a smaller group of 99 patients, was presented by Zhou et al in 2022[32]. They compared the effects of hyaluronic acid and PRP combined with hyaluronic acid - 45 patients were treated with HA and 54 with the combination preparation. The effects were evaluated 5 weeks after a single injection preceded by arthroscopic debridement, using VAS and Lysholm (LKS) scales and measuring inflammatory cytokines. The combination of the two substances reduced inflammatory markers more than acid alone. The plasma also obtained better functional scores according to the Lysholm scale, but a weaker analgesic effect according to the VAS.

Another interesting observation of the researchers was the better response to treatment in young people with lower BMI.

Similar results were obtained by Xu et al. in a prospective cohort study comparing HA, PRP and HA + PRP[33] . The 122 cases of knees affected by osteoarthritis were divided into 3 groups. Each received 3 injections and the effect was evaluated at 2, 6, 12 and 14 months using the VAS, WOMAC, Lysholm and Lequesne scales. In addition, inflammatory indices and synovial membrane and cartilage recovery were monitored using Doppler ultrasound. In all areas tested, the combined formulation showed the highest efficacy - reducing pain, increasing function, improving synovial membrane quality and having a better anti-inflammatory effect than either PRP or HA alone.

Not only PRP, but also hyaluronic acid preparations may differ in composition. The purpose of the 2021 study by Sun et al. was to evaluate the efficacy of cross-linked HA in combination with PRP and compare it to PRP alone[34]. Cross-linked HA degrades much more slowly than regular hyaluronic acid salt. The study group consisted of 85 subjects who received only one injection. Evaluation of results was based on VAS, WOMAC, Lequesne, Single Leg Stance Index scales. Initially, PRP alone produced better results - it had a better analgesic effect when evaluated one month after injection. However, in the long term, a mixture of preparations proved to be better at reducing pain.

The majority of studies on PRP therapy have focused on knee osteoarthritis, with relatively few investigating its effects on other joints. One notable exception is a randomized controlled trial by Paget et al.[41], which examined PRP in patients with ankle osteoarthritis. The control sample consisted of subjects who received saline injections. There were a total of 100 subjects, each receiving 2 injections 6 weeks apart. After 52 weeks, there was no significant difference in outcomes and the effect of PRP was similar to placebo. However, it is important to note that most patients with ankle osteoarthritis in the study were young and had a history of trauma. Additionally, the authors did not specify the method of PRP preparation or its composition.

Conclusions

Osteoarthritis is a major public health concern, particularly in aging populations. Its consequences are deeply felt in daily life and have a significant impact on patients' quality of life. The lack of effective treatments-especially those capable of halting or slowing disease progression-remains a source of frustration for both patients and clinicians. This highlights the urgent need to explore new therapeutic approaches that are not only effective and safe but also address the underlying pathophysiological mechanisms of the disease.

Several studies included in this review point to the potential benefits of autologous platelet-rich plasma (PRP) injections in the treatment of osteoarthritis. PRP has been shown to reduce pain, improve joint function, and enhance the quality of the synovial membrane. While the clinical outcomes are not dramatic, they stand out in the context of limited existing treatment options and suggest that PRP may serve as a valuable adjunct in osteoarthritis management. A critical issue that emerges, however, is the need for standardization of PRP preparation protocols. The literature indicates that variables such as centrifugation speed, duration, and the presence of leukocytes significantly influence the biological activity and therapeutic efficacy of PRP. Most studies suggest that leukocyte-poor PRP (LP-PRP), which minimizes inflammatory cell content, is associated with better outcomes.

Moreover, recent research points to the potential benefits of combining PRP with other agents, particularly hyaluronic acid (HA). The combination of PRP and cross-linked HA may not only enhance the therapeutic effect but also extend its duration. This approach could be especially beneficial in patients with more advanced degenerative changes.

Another area requiring further development is the optimization of dosing regimens. Evidence suggests that treatment should be tailored to the severity of the disease. Patients with early-stage osteoarthritis may respond well to a single injection, with effects lasting for several months, whereas those with more advanced joint degeneration often require repeated injections at shorter intervals. Despite promising findings, there is still a notable lack of high-quality studies investigating PRP use in joints other than the knee. While the majority of clinical trials have focused on knee osteoarthritis, data on the ankle, hip, or shoulder remain limited, underscoring the need for broader, joint-specific research.

It is important to recognize that PRP alone is unlikely to serve as a base of treatment for osteoarthritis. Comprehensive disease management requires a multimodal approach, integrating timely and appropriate physical activity, weight management, and pharmacologic pain control. Nevertheless, the continued refinement of PRP preparation and administration protocols may contribute to improved disease control, better functional outcomes, and reduced dependence on systemic medications.

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