



The Use of Platelet-rich Plasma in the Treatment of Osteoarthritis: A Narrative Review

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ABSTRACT

Osteoarthritis is a degenerative chronic joint disease characterized by mechanical inflammation of the synovial membrane and damage to articular cartilage, with pain as the main symptom. Conservative treatment focuses on alleviating the symptoms and improving the quality of life. Paracetamol and other non-steroidal anti-inflammatory drugs, which patients often take to relieve pain, can cause various side effects. Therefore, intra-articular injections have been increasingly used recently and have shown good results. Most used are injections based on corticosteroids, hyaluronic acid and platelet-rich plasma (PRP), with PRP being the newest method. The aim of this article is to review the relevant literature to present the latest findings regarding the preparation, application and efficacy of PRP in osteoarthritis and the effects of combining PRP with other forms of biological and conservative treatment as a possible new and more successful method of treating osteoarthritis. A comprehensive literature search was conducted in the PubMed and Scopus databases using specific keywords. To ensure that only high-quality evidence was included, only randomized controlled trials, meta-analyses and narrative reviews published in English between 2010 and 2024 were considered. There are many factors that make each PRP unique, making it difficult to prove its absolute effectiveness with certainty. Currently, increasing research is being conducted on combination therapy, as it has been shown that it may provide better results than PRP, hyaluronic acid or corticosteroids alone. In conclusion, PRP has shown promising results as a potential new and more successful method of treating osteoarthritis.



1. INTRODUCTION

Degenerative changes to joints affect many people over 65 years of age and, if left untreated, can pose a major problem in performing activities of daily living. Osteoarthritis is the most common degenerative and chronic joint disease in which there is a mechanical inflammatory reaction of the synovial membrane and damage to the articular cartilage. The hip and knee joints are most affected, but the carpometacarpal joint of the thumb, the elbow and other joints can also be affected [1, 2]. The treatment of osteoarthritis is predominantly conservative and symptomatic [2]. Considering that patients often take paracetamol or some non-steroidal anti-inflammatory drugs, which can cause various side effects, this article focuses on newer treatment methods with intra-articular injections, which have been shown to be very effective in relieving pain. Most used are corticosteroids and

hyaluronic acid, and the newest method is platelet-rich plasma (PRP) preparation. This is an autologous platelet concentrate that is obtained by centrifuging the patient's blood. By releasing growth factors, it has an anti-inflammatory effect and stimulates the anabolism of the synovium and articular cartilage [1]. The preparations differ from each other depending on whether they contain leukocytes or not, as well as in the dosage, potency, purity and activation method of the preparation. Due to these differences and the lack of consensus on the preparation procedure and relatively short duration of clinical use, it is difficult to prove the absolute efficacy of these methods with certainty [3–5].

The aim of this article is to review the relevant literature to present the latest findings regarding the preparation, application and efficacy of PRP in degenerative joint changes and the effects of

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combined PRP and hyaluronic acid therapy as a possible new and more successful method for the treatment of osteoarthritis, which has shown promising results so far.

2. METHODS

2.1. Review Objective and Eligibility Criteria

The target population for this review are adults aged 18 years and over who have been diagnosed with osteoarthritis. To ensure the inclusion of high-quality evidence, only randomized controlled trials, meta-analyses and narrative reviews published in English between 2010 and 2024 were considered.

2.2. Search Strategy

A comprehensive literature search was conducted in PubMed and Scopus using specific keywords and terms, including: Osteoarthritis AND Platelet Rich Plasma; Osteoarthritis AND Platelet Rich Plasma AND ((Knee) OR (Hip)); Platelet rich plasma AND Osteoarthritis AND ((Hyaluronic acid) OR (Corticosteroid injection)).

Filters were applied to restrict results to randomized controlled trials, meta-analyses and narrative reviews published between 2010 and 2024.

2.3. Study Selection Process and Data Synthesis

The initial screening process involved a review of titles and abstracts to identify potentially relevant studies, which were later evaluated and their data extracted and added into a cohesive summary.

2. Conservative Treatment of Osteoarthritis

The treatment of degenerative joint changes is aimed primarily at relieving pain but also at increasing the range of motion of the joint and strengthening the muscles. Clinical guidelines for the management of knee and hip osteoarthritis recommend conservative non-pharmacological treatment before drug therapy and surgery. This treatment method places particular emphasis on patient education and therapeutic exercises. For people with hip osteoarthritis, reducing their body weight is very important [2].

Physical inactivity is not only a risk factor for osteoarthritis but also a symptom of the disease that leads to pain and stiffness in the affected joint. As a result, most patients have difficulty performing activities of daily living, which leads to a reduced quality of life. For this reason, physical activity is one of the recommended ways to deal with the changes in joints [6].

The treatment of osteoarthritis usually begins with the onset of symptoms when the disease is already advanced [7]. In addition to therapeutic exercises, manual therapy is often used. Muscle stretching, manipulation and manual traction have positive effects, especially in patients with hip osteoarthritis. Electrotherapeutic procedures are used more frequently for treating knee osteoarthritis. Transcutaneous electrical nerve stimulation (TENS) can be used at all stages of the disease. Therapeutic ultrasound has both thermal and non-thermal effects and increases the pain threshold. Laser therapy can also be used to relieve pain, and magnetic therapy can further reduce stiffness and improve function [8]. Both cryotherapy and thermotherapy have positive effects on hip and knee osteoarthritis. Locally applied cryotherapy is used in the acute phase of the disease, whereas thermotherapy is used for chronic pain. Both forms have a pain-relieving effect [7–9]. Some patients also use complementary methods such as yoga, tai chi or acupuncture, although their effectiveness still needs to be investigated further [7, 10–12].

In addition to education and exercise, patients should also follow a good nutritional program, as the combination of these approaches has been shown to be successful in improving function and symptoms as well as reducing pain [13].

Pharmacological agents used in the treatment of osteoarthritis of the hip and knee can be applied locally, by intra-articular injection, or can be taken orally. Non-steroidal anti-inflammatory drugs (NSAIDs) can be taken orally and play a role in relieving symptoms. Paracetamol is taken initially, and diclofenac and etoricoxib are considered to be the most effective. However, due to the risk of cardiovascular disease and gastrointestinal symptoms, it is recommended that these patients receive the lowest possible dose and for the shortest possible period of time. Recently, interest in biological therapy has increased. Orthobiologics, including hyaluronic acid preparations and platelet-rich plasma preparations can be injected intraarticularly [1, 13].

3. Platelet-rich Plasma

Platelet-rich plasma (PRP) is a preparation that is obtained by centrifuging the patient's blood and can be applied to a joint affected by degeneration. By releasing growth factors and cytokines, it reduces inflammation and promotes regeneration [3]. PRP can induce regeneration, which leads to an improvement in the metabolic functions of damaged structures [14].

3.1. *Biological Properties of Blood Platelets*

It was assumed that the primary role of platelets was to maintain hemostasis, thrombosis and wound healing. In recent years, however, scientific research and new technologies have provided new perspectives on platelets and their functions, such as their possible role in immunity. Platelets also contain many growth factors and cytokines that influence inflammation, angiogenesis, stem cell migration and cell proliferation [4, 15].

3.2. *Structure, Application and Types of PRP Preparation*

The structure of PRP itself varies, and there is no exact or agreed-upon method for preparing PRP and concentrating the components in the blood. There are currently many different PRP systems on the market. Accordingly, different preparation protocols exist depending on the manufacturer, which gives each PRP unique properties. The preparations differ depending on the isolation method (whether the preparation is centrifuged once or twice), the centrifugation speed and the type of system used. Regardless of the variations, blood is first drawn from the patient, and this blood is mixed with an anticoagulant prior to centrifugation [3]. In the next step, the blood is placed in a centrifuge, where the centrifugal force causes the individual cell components to sediment due to their different densities. Centrifugation "separates" the blood into several layers so that the preparation has a layer with red blood cells, a layer with platelet-poor plasma (PPP) and a "buffy coat", i.e., a layer with concentrated platelets and leukocytes [3]. The layer with the red blood cells is then separated and centrifuged a second time. After the second centrifugation, the middle layer is removed as a PRP preparation, and the platelet concentration is greater than 1000×10^3 platelets/ μL [5]. The resulting preparation can finally be injected directly into the patient's body or additionally "activated" beforehand by adding either calcium chloride or thrombin, which causes platelet degranulation and the release of growth factors [3]. Although there is evidence supporting the use of PRP, the constant dose and the exact method of preparation are not yet standardized. Bansal et al. concluded that a dose of 10 billion platelets in 8 mL of PRP improves a person's functional ability, reduces symptoms and protects cartilage from further damage, whereas a smaller volume of PRP with 10 billion platelets achieves the same result [16]. Several authors have attempted to categorize PRP on the basis of some of its properties, method of preparation and application, but there is still no generally accepted classification

[4]. PRP can be divided into two main categories according to whether leukocytes are included in the preparation. The first is pure PRP, which contains no leukocytes, and the second is LR PRP (leukocyte-rich PRP), which contains leukocytes. The latter is associated with a proinflammatory effect due to a greater number of catabolic cytokines [3]. There is another categorization of PRP, the DEPA classification (i.e., dose, efficiency, purity, activation), which is based on these four different components [4].

4.3. *Side Effects and Contraindications*

Even though the application of PRP is a minimally invasive technique, there are some possible side effects and contraindications that should be considered. Some of the potential side effects include the possibility of injection site morbidity, the formation of scar tissue and calcification at the formation site, allergic reactions and rare infections at the site of injury. Furthermore, there are contraindications to the use of PRP in individuals diagnosed with sepsis, acute and chronic infections, anticoagulation therapy, platelet dysfunction syndromes, thrombocytopenia and others [14].

4. *Comparison of PRP with Other Treatment Approaches*

There is currently no causal treatment option for osteoarthritis, but therapy is limited to alleviating symptoms [17]. Conventional treatment methods include physiotherapy, pain-relieving and anti-inflammatory drugs, hyaluronic acid, PRP and intra-articular corticosteroid injections [18].

Non-steroidal anti-inflammatory drugs and paracetamol are used to relieve pain in osteoarthritis patients. However, their continuous use is not recommended because of possible cardiovascular and gastrointestinal side effects. This is a particular problem for people with comorbidities, which is often the case here [19]. For this reason, intra-articular injections could be a very good treatment option, as the side effects are reduced by direct application to the affected tissue [19, 20]. Corticosteroids, hyaluronic acid, PRP, mesenchymal stem cells and ozone therapy have proven to be the most commonly used agents. For PRP itself, as well as for mesenchymal stem cells, there is currently limited evidence to support their use, but it should be considered that they represent a new method in the treatment of degenerative joint changes compared with corticosteroids and hyaluronic acid [19].

5.1. The Effectiveness of PRP Compared with Other Intra-articular Injections

Corticosteroids are hormones that occur naturally in the human body and are synthesized in the adrenal cortex. This group of hormones includes glucocorticosteroids such as cortisol, which primarily have anti-inflammatory and immunosuppressive effects, and mineralocorticosteroids such as aldosterone, which influence sodium reabsorption and potassium secretion. The intra-articular administration of corticosteroids is probably the most common conservative method for treating knee osteoarthritis and has been used for more than 50 years. Osteoarthritis is primarily a degenerative disease of the joints, but in some stages of the disease, there is also mild inflammation. Corticosteroids also have anti-inflammatory effects, acting at multiple cellular levels by blocking the synthesis of proinflammatory signaling molecules such as interleukin 1 and prostaglandin. The analgesic effect of NSAIDs as injections is better than that of oral NSAIDs [19, 20].

Hyaluronic acid is a glycosaminoglycan that functions as a lubricant and for shock absorption in joints. As its concentration is reduced by 33–50% in people with osteoarthritis, its use is generally recommended [19]. The injections not only lubricate the joint but also have a mechanical and biomechanical effect that is not immediate but long-term [21]. It is effective for up to 26 weeks and is considered a better option for treating degenerative changes than corticosteroid injections [19].

PRP affects the cellular environment by releasing growth factors and immunomodulatory molecules that may play important roles in reducing inflammation and stimulating the anabolism of the synovium and articular cartilage. Most studies have shown that PRP is a better therapy than hyaluronic acid, especially in milder cases of osteoarthritis. However, many researchers have obtained contradictory results in its application, which could be due to different preparation methods and the fact that each preparation differs from the previous one due to the human factor [19].

Raeissadat et al. conducted a study with 283 patients in which knee osteoarthritis was assessed via the Lequesne index, the visual analogue scale (VAS) and the WOMAC. The patients were divided into four groups, each of which received a different form of intra-articular injection. The first group received three doses of hyaluronic acid in one week, the second group received two doses of PRP at three-week intervals, the third group received three doses of plasma rich in growth factors (PRGF) and the fourth group received three doses of ozone per week. The evaluations were performed two, six and

twelve months after the injections. Two months after the applications, all four groups, especially the ozone group, presented significantly lower Lequesne index, WOMAC and VAS scores compared to the pre-application results. However, the effect of ozone completely disappeared 12 months after application, indicating a strong but very short-term effect (4–6 months). After six months, patients treated with hyaluronic acid, PRP and PRGF had better results than those treated with ozone, although the difference between them was not statistically significant. After one year, patients treated with PRP and PRGF showed significantly better results than patients treated with hyaluronic acid or ozone. The reason for this is the destruction of hyaluronic acid at the site of inflammation, while PRP and PRGF stimulate chondrogenesis and proliferation, which prolongs their effects [22]. Similar results were obtained by Duymus et al., who compared the efficacy of hyaluronic acid, ozone therapy and PRP. After one month, significant progress in the WOMAC and VAS scores was observed in all the groups. After three months, ozone therapy had worse results. After six months, the effect of ozone therapy had completely disappeared, whereas the results were similar for hyaluronic acid and PRP, and after one year, PRP proved to be clinically and statistically significantly better than hyaluronic acid. PRP has thus proven to be an effective method for the treatment of mild to moderate knee osteoarthritis, enabling pain-free performance of activities of daily living for at least one year [23]. In their meta-analysis, Tang et al. compared the efficacy of PRP with that of hyaluronic acid and came to a similar conclusion: PRP is more effective in reducing pain and improving functional activities in the short and long term [24]. Chen et al. also concluded that PRP had greater efficacy in reducing pain and improving function in patients with knee osteoarthritis than did hyaluronic acid or placebo for up to one year [25]. On the other hand, Phillips et al. reviewed the literature and concluded that the intra-articular application of corticosteroids and hyaluronic acid is recommended for the treatment of knee osteoarthritis, but evidence to recommend or reject PRP as a treatment method is lacking [26].

5.2. The Effectiveness of PRP in Combination with Other Forms of Biological and Conservative Treatment

According to some sources, combined therapy has proven to be more effective than using only one type of intra-articular injection. Thus, the use of both corticosteroids and hyaluronic acid provides better short-term and long-term results in reducing pain, and PRP in combination with

hyaluronic acid is more effective than PRP alone or hyaluronic acid alone; however, combination therapy should be proposed with caution [19]. Nouri et al. compared the effects of PRP, hyaluronic acid, and their combination in people with mild to moderate hip osteoarthritis. Compared with the start of treatment, all three types of interventions led to a reduction in pain and improvement in function and significant differences in the WOMAC score, VAS score and Lequesne index score at 2 and 6 months after application. The group with PRP and PRP in combination with hyaluronic acid showed better results than the group with the application of hyaluronic acid alone, but there were no significant differences between PRP alone and the combined therapy, but a small number of studies have been performed on this topic, and more research should be done to better investigate the effectiveness and safety of the application [27]. Similar conclusions were reached by Zhao et al., who, through a systematic review, concluded that PRP in combination with hyaluronic acid may have promising clinical effects in the treatment of knee osteoarthritis. Compared with PRP and hyaluronic acid alone, the combined therapy had greater effects on the WOMAC score, VAS score and Lequesne index score, but the difference was not significant, and all three methods were proven to be effective [28].

Raeissadat et al. investigated the efficacy of therapeutic exercise compared with the combination of PRP with therapeutic exercise. The study included 46 patients with stage 1, 2 and 3 osteoarthritis and used the VAS, WOMAC and MRI to assess four characteristics of the knee: patellofemoral cartilage volume, subarticular bone marrow abnormalities, lateral and medial meniscus integrity and the presence or absence of synovitis. The PRP used in this study contained leukocytes (LR-PRP), and the platelet concentration was 4–6 times greater than normal. In the experimental group, PRP was applied, and one week after the injection, the participants started therapeutic exercises. The control group started the exercises immediately. At the end of the study, the VAS score significantly improved between and within the groups. There was also a large difference in the WOMAC score between the two groups. In the PRP group, the patellofemoral cartilage, synovitis and integrity of the lateral and medial meniscus improved substantially after treatment, whereas in the control group, only the patellofemoral cartilage volume showed meaningful improvement [29]. Thus, the combination of PRP and therapeutic exercises has proven to be a very successful method for the treatment of osteoarthritis, which should be investigated further.

More recently, the connection between the consumption of certain drugs and the application of PRP has also been investigated. In a systematic review, Kao et al. concluded that certain medications such as paracetamol and aspirin can negatively influence the effectiveness of PRP by reducing the number and function of blood platelets. They concluded that aspirin, paracetamol and non-selective NSAIDs should not be taken before PRP injection. On the other hand, selective cyclooxygenase 2 (COX-2) inhibitors, can be safely consumed. However, studies describing the effects of paracetamol on platelets are contradictory, so further research on this topic is needed [30].

5. Conclusions

When conservative treatment of osteoarthritis no longer has the desired effect, the focus was previously placed exclusively on surgical procedures. Today, the focus is increasingly shifting to regenerative medicine, primarily through the use of intra-articular injections based on corticosteroids, hyaluronic acid and the preparation of platelet-rich plasma (PRP), of which the latter method is the most recent. In the treatment of osteoarthritis, PRP has proven to be very effective in relieving pain and is a better option than non-steroidal anti-inflammatory drugs, as the direct application of PRP reduces side effects. It has been shown to be more effective than other intra-articular injections, but some studies suggest that combined therapy achieves even better results. Compared with patients who received corticosteroids, patients who received intra-articular PRP or hyaluronic acid achieved better long-term results in terms of pain relief and improvements in activities of daily living; however, even better results were achieved by those who received both PRP and hyaluronic acid. Combined therapy should always be approached with great caution, but it shows promising results as a possible new and more successful method for treating degenerative joint changes, which leaves many possibilities for further research.

Conflict of Interest

No conflict of interest is declared by the authors. In addition, no financial support was received.

Ethics Committee

The study did not follow protocol as per the guidelines of the Ethics Committee because it is a narrative review.

Author Contributions

Conception and design of the study: LV, DK; Data collection: LV; Data analysis: LV, DK; Data Interpretation: LV, DK; Drafting the article and/or its critical revision: LV, DK; All authors have read and agreed to the published version of the manuscript.

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