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Rich in Platelets but Poor in Certainty? Current Evidence on Platelet-Rich Plasma Injections for Osteoarthritis

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Abstract

This integrative review evaluates the effectiveness of platelet-rich plasma (PRP) injections in treating patients with chronic pain secondary to osteoarthritis (OA). A comprehensive review was performed, incorporating 13 peer-reviewed clinical trials, systematic reviews, and meta-analyses evaluating PRP for OA treatment. These studies focused primarily on comparing the efficacy and safety of PRP to other forms of analgesia and the effects of these medications on disease progression. Evidence suggests that PRP injections provide clinical benefit in patients with mild to moderate OA. Some studies demonstrate superior or comparable efficacy compared with other common forms of OA analgesia, including corticosteroid injections, hyaluronic acid injections, and nonsteroidal anti-inflammatories. PRP may additionally have disease-modifying effects to reduce the loss of cartilage in patients with OA, although this has not been definitively established. In addition, a reduction in analgesic burden after injection of PRP has not been demonstrated. Limitations remain in the study of PRP efficacy to include selection bias, short-term studies, inconsistent formulations of PRP, and differing injection techniques. Future research should focus on eliminating these limitations to allow for more certain recommendations regarding PRP injections. After over a decade of use, PRP injections remain a reasonable alternative for treating patients with OA but not a definitively better one.

Introduction

Osteoarthritis (OA) is one of the primary causes of chronic pain in adults, and estimates predict that cases of OA will increase leading up to 2050[1]. OA is a type of degenerative joint disease, and it is the most common form[2]. It degenerates cartilage, resulting in the formation of osteophytes and subchondral sclerosis or scarring. Although cartilage is a critical component of the pathophysiology, there are many proinflammatory cytokines that are found in the synovial fluid of joints with OA. This observation supports that the synovium is affected as well. This is key to the newer perspective of the pathogenesis of OA as a chronic inflammatory response rather than the classic wear and tear theory[2]. These cytokines lead to inflammatory responses that result in the structural changes observed in OA-affected joints.

Pain resulting from OA is currently managed clinically with medications such as nonsteroidal anti-inflammatory drugs (nonsteroidal anti-inflammatories [NSAIDs]), steroids, benzodiazepines, acetaminophen, and opioids. According to a 2020 study, approximately 27% of visits for treating patients with a primary diagnosis of OA included prescription opioids and benzodiazepines[3]. This suggests that OA may be contributing to the broader opioid crisis by increasing the number of opioid prescriptions. As a result, it is becoming increasingly important that alternative and effective

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measures for pain management of OA are developed.

Platelet-rich plasma (PRP) injections have been demonstrated to be effective in decreasing pain, increasing quality of life, and improving function after administration for OA[4]. Similarly, the use of PRP injections has been illustrated to relieve pain for temporomandibular joint osteoarthritis and other orthopedic applications such as lateral epicondylitis and patellar tendonitis[5,6]. There is also hope that PRP may be disease-modifying, specifically with respect to reducing cartilage degeneration in patients with OA. However, there is a gap in knowledge regarding whether PRP injections are effective enough to decrease the use of additional pain medications such as opioids and NSAIDs. This is crucial to evaluate for patients looking for pain relief without undergoing total joint replacement.

Another important reason to identify effective alternatives includes the side effects of currently used medications. For example, NSAIDs are associated with well-documented adverse side effects such as acute kidney injury and gastric ulcers[7]. This integrative review will seek to address the current knowledge gap by communicating the current findings in literature regarding the analgesic effect of PRP injections compared with other pain relief modalities.

A comprehensive search methodology was used in the creation of this work, incorporating 13 peer-reviewed clinical trials, systematic reviews, and meta-analyses published between 2020 and 2025. Artificial intelligence was used sparingly in the creation of this article. It was used to assist with reference structure, ensure clarity of writing, find relevant research studies, and ensure accuracy of information (Appendix 1). However, all recommendations from artificial intelligence were reviewed personally and checked for accuracy before inclusion in this work.

Discussion

This integrative review begins with a brief overview of how PRP injections are created and function, which matters clinically for better educating patients. Second, the review examines the effectiveness of PRP injections in treating pain associated with OA in the knees and hips, which are common sites of OA[8]. Third, the effects that PRP has on the cartilage of the joints themselves are examined. Finally, PRP is compared with other commonly used analgesics based on both efficacy and risk profile.

Mechanism of Action

PRP is obtained from platelet concentrate that is derived from autologous whole blood[9]. The blood sample is collected from the patient and centrifuged to concentrate the platelets. There are several formulations that are generated during this process, and each has its own unique effects and applications[2]. Examples include pure PRP, leukocyte-rich PRP, pure platelet-rich fibrin (PRF), and leukocyte-rich PRF. This variability matters because each should be used differently depending on the desired application and to promote optimal outcomes. For example, PRF has a natural clotting process and does not require activators, while PRP needs additional components added to it to form a clot. In addition, leukocyte-rich formulations of PRP and PRF reduce infection rates and have been demonstrated to be important in angiogenesis[10]. However, leukocytes have also been shown to impair the overall efficacy of PRP due to the release of lytic enzymes and proteinases[11]. This demonstrates the importance of the formulation used depending on the desired effects.

Additional components required to activate PRP include calcium chloride or collagen from damaged tissues, much like platelets are activated naturally after blood vessel injury[2]. This activation results in a complex release of cytokines and growth factors that can influence inflammation and repair in joints affected by OA[2]. Previous studies using PRP to treat OA have demonstrated potential benefits from this biochemical process, including decreasing negative gene expression, decreasing proinflammatory markers, and improving functional and pain scores[2].

Effects of PRP on Cartilage Tissue

Despite interest from the medical community regarding whether PRP can regenerate cartilage, limited evidence exists to demonstrate clinically significant results. Magnetic resonance imaging (MRI) has been demonstrated as an effective imaging modality to measure the degree of OA and the improvement from treatment modalities. However, a consensus has not been reached regarding the effects of PRP on cartilage loss. There are inconsistent results regarding this, with some showing promising effects on cartilage and others demonstrating a lack of evidence of cartilage preservation using MRI[4]. Studies that demonstrated improved cartilage thickness and synovitis following PRP injections on follow-up MRI suffered from limitations[12,13]. These included small study sizes, questionable results regarding cartilage regeneration or simply a slower rate of degeneration, differences in study populations regarding sex, body mass index, and pretreatment OA severity, and inconsistent use of leukocyte-rich vs. leukocyte-poor PRP formulations. As a result, much of the interest regarding the "regenerative" effects of PRP on cartilage tissue remains speculation rather than scientifically demonstrated fact.

The Effectiveness of PRP Injections for OA

Knee OA

Knee OA is a chronic, slowly progressing condition that burdens patients both by the pain it causes and the lack of effective treatments to stop its progression. PRP injections have shown effectiveness relieving pain in patients with knee OA, as many demonstrated stable improvement in clinical scores for up to 24 months when compared with those injected with

sham saline[11]. Using the Western Ontario and McMaster University Osteoarthritis index (WOMAC) scores, this study demonstrated an improvement by 27.1 points after 24 months in the PRP group when compared with the sham saline group[11]. PRP injections have also been shown to relieve pain and improve other common knee OA functional scores such as the Knee Society Score and Visual Analog Scale (VAS)[4]. For example, one study found that the functional Knee Society score of patients with knee OA improved in a statistically significant way by approximately 10 points 6 months after injection with PRP[4]. In addition, the same study also demonstrated an improvement in VAS score by approximately 3 points in patients with knee OA 6 months after treatment with PRP[4].

Despite these findings, additional questions regarding PRP in treating knee OA remain. While these studies primarily focused on PRP treating knee OA of the tibiofemoral articulation, it is unclear if PRP is effective in treating patellofemoral knee OA. The isolated form of patellofemoral knee OA affects 8% to 24% of the general population[14]. A systematic review of PRP injections for patellofemoral knee OA found that these intra-articular injections may result in a steady trend of benefit clinically[14]. This included significant improvement in WOMAC and VAS pain scores as demonstrated previously. Specifically, it was demonstrated that the VAS score decreased from 7.5 to 1.0 and the WOMAC score from 18.3 to 7.3, indicating statistically significant improvements in pain following PRP injections[14].

It is also unclear whether repeat injections of PRP provide additional symptomatic relief. A study by Zhuang et al.[15] found that over time, patients who received 3 or 5 injections experienced more relief than those with only one injection. Once again using WOMAC and VAS scores, it was demonstrated that patients receiving one PRP injection started experiencing increasing pain scores after 6 weeks, while patients who received 3 or 5 injections did not start showing a substantial increase in pain scores until 24 weeks[15]. However, there was no significant difference in the results between those who received 3 injections and those who received 5.

Hip OA

Beneficial effects of PRP for the treatment of hip OA have been demonstrated both in small pilot studies and larger reviews. In a small study evaluating the effects of PRP on early hip OA in 9 patients, PRP improved patient-perceived functionality scores[16]. Functionality scores that were used included the modified Harris hip score, hip outcome score-activities of daily living subscale, and a short version of the International Hip Outcome TOOL called iHOT-12. Each one of these scores had a statistically significant improvement over a span of 12 months following injection[16]. VAS pain scores did decrease by 1.7 points at 3 months, but this was statistically insignificant[16].

In a larger review study of PRP for treating hip OA, however, there was a statistically significant improvement in pain but not functionality[17]. The improvement in pain lasted less than 6 months in duration. These studies similarly used VAS scores for pain and hip outcome score-activities of daily living subscale and Harris Hip Score for functionality[17]. This demonstrates inconsistencies depending on the population of the studies, and it must be clarified before making broad scale recommendations regarding PRP for treating hip OA. While beneficial effects of PRP for treating patients with hip OA have been demonstrated, current studies are inconsistent in determining improvement in pain, functionality, and durability.

Comparing PRP with Other OA Treatments

Comparing Beneficial Effects

When comparing the effects of PRP in reducing OA-related pain with other modalities, results have been mixed yet promising. Several studies regarding injections of PRP in the treatment of OA have demonstrated superior or comparable WOMAC and VAS scores when compared with hyaluronic acid (HA), corticosteroids, NSAIDs, and placebos[18,19]. However, a systematic review and meta-analysis evaluating these findings suggested that methodological flaws were present, specifically citing selection bias, small sample sizes, and low quality of evidence[20]. There is primarily low quality evidence supporting the claim of superior pain relief with PRP compared with other forms of analgesic treatment in patients with OA[20]. In addition, research has yet to demonstrate a reduction in analgesic burden after using PRP to treat OA-related pain. As a result, future studies should focus on reducing these limitations so that the medical community can make a more substantial recommendation regarding the efficacy of PRP against other OA treatments.

Comparing Adverse Effects

The safety profile of PRP when compared with other common analgesic therapies for OA remains an important consideration. When comparing the types of PRP injection, leukocyte-rich formulations have been shown to have the highest percentage of adverse events[21]. The most common adverse event was pain, followed by swelling and transient febrile reactions. However, 91.2% of these symptoms resolved within 72 hours without additional treatment required[21]. When compared with other modalities, PRP was less likely to be associated with accelerated cartilage loss such as steroid injections, and it had significantly fewer adverse effects than NSAIDs. PRP injections did show mildly elevated local injection-site reactions when compared with HA injections. In addition, it is important to note that patients older than 65 years were more likely to experience adverse effects. Overall, PRP is considered a relatively safe

treatment modality, which is often ascribed to its autologous nature.

Steroid injections have become nearly synonymous with treatment for arthritic joints, but they carry risks as well. A preclinical review study evaluating the effects of steroids on cartilage found beneficial effects macroscopically but detrimental effects histologically[22]. This demonstrated that detrimental effects on cartilage are difficult to prove, similar to the difficulty in proving PRP has beneficial effects on cartilage. Other studies suggest that cortisone can decrease cartilage tissue in humans. In one study, subjects with knee OA who were treated with cortisone injections showed a statistically significant additional loss of 0.1 mm of cartilage over a 2 year span when compared with controls[23]. Similarly, cortisone injections are associated with increased rates of total knee replacements and shorter time to arthroplasty[23]. Another study stated that systemic steroids could increase the incidents of deep vein thrombosis, sepsis, and fracture[24]. Specifically, 5 of every 1,000 steroid users developed deep vein thrombosis, 2 of every 1,000 users developed sepsis requiring hospitalization, and 21 of every 1,000 users suffered a fracture[24].

Although commonly used to treat chronic pain in OA, there are many risks associated with the chronic use of NSAIDs[7]. NSAIDs have been demonstrated to exert adverse effects on the cardiovascular, renal, and gastrointestinal systems. However, this is well demonstrated to be due to the frequency of use in treating pain rather than NSAIDs being a particularly high-risk class of medications[7]. It is also important to note that topical formulations have significantly less systemic absorption, which can greatly decrease adverse effects.

Opioid use in treating OA is associated with distinct adverse effects when compared with those associated with NSAIDs and steroids. This is prominent due to the effects on the central nervous system, although this is not exclusive. A meta-analysis performed in 2019 identified many adverse effects associated with opioids, including central nervous system effects, constipation, loss of appetite, nausea and vomiting, pruritus and rashes, and oral ulcerations[25]. It has also been demonstrated that opioids decrease the variability of gait with ambulation, possibly increasing the risk of falls while on these medications[26]. One study found that opioids were not clinically better than placebo at providing at least 50% of pain relief or more in patients with OA[27]. This suggests that the variable pain relief seen in patients with OA may not be worth the risk trade-off.

Strengths and Limitations

The strengths and limitations of this integrative review are important for proper application of its findings. One specific strength is the integrative review design, which generally allows for identification of knowledge gaps and versatile literature analysis. Similarly, the growing number of recent studies provides a substantial database from which to draw conclusions regarding PRP risks, benefits, and clinical applications for OA. While these strengths allow for a thorough evaluation of the current knowledge of PRP for treating OA, there are many limitations remaining. Many of the studies cited point out that they are limited by several factors. First, there are variations in use of leukocyte-rich vs. leukocyte-poor formulations of PRP between studies. Second, severe OA cases were often omitted when establishing the study populations. Third, some PRP injections were ultrasound-guided while others were not. Finally, long-term effects have not been adequately demonstrated due to a lack of data in this area. These limitations are important to consider when making an accurate interpretation of the data presented.

Future Research Suggestions

The limitations identified in this review help make informed decisions regarding future research. First, there need to be studies that evaluate whether the use of PRP injections for OA treatment decrease the need for other forms of treatment, as there are not any such studies at the time of this writing to the author's knowledge. Long-term effects of PRP need to be further elucidated in future research. Consistent formulations need to be used in studies to better apply the results. In addition, many studies at this time have only researched PRP for mild-to-moderate OA severity, and PRP needs to be studied for use in severe OA. Addressing these gaps in knowledge would strengthen the current knowledge base and assist in clarifying an evidence-based recommendation of PRP vs. other analgesic treatments for OA-related pain.

Summary

This integrative review has demonstrated several significant findings regarding PRP treatment for OA. Evidence supports that injections of PRP for treating knee OA are associated with improvements in both pain and functional scores. By contrast, treatment of hip OA with PRP injections has been inconsistent in its findings regarding whether it improves pain scores, functionality, or both.

Although there is continued interest surrounding the possible regenerative effects of PRP in treating cartilage loss, this has not been definitively demonstrated in a clinically meaningful way. When compared with HA injections, steroid injections, NSAIDs, and placebo, PRP injections may provide superior or comparable benefits; however, these studies do have significant limitations with regard to methodological weaknesses and heterogeneity. In addition, PRP injections may have a more optimal risk profile when compared with other pain treatment modalities such as steroids, NSAIDs, and opioids. Overall, current evidence suggests that PRP injections can be beneficial in treating OA. However, the recommendation is that PRP should not be considered

definitively more beneficial or superior for all OA-related pain at this time. Clinicians should consider PRP as a valuable option for the care of patients with OA-related pains in cases of mild to moderate severity.

Conclusion

This integrative review evaluates PRP injections for treating patients with chronic pain secondary to OA. OA is a major cause of chronic pain worldwide, and current pain-relief options have significant drawbacks. These include adverse effects on many of the body's vital organ systems, including the renal, gastrointestinal, and cardiovascular systems. In addition, many patients do not find significant relief from current conservative measures and feel limited in their options outside of surgical intervention. As a result, there is a substantial need for additional conservative modalities for relieving OA-related pain.

This integrative review suggests that PRP shows clinical efficacy in treating common sites of OA, primarily when the disease is mild-to-moderate. PRP also demonstrates comparable or superior outcomes when compared with other pain-relieving modalities such as steroids, HA injections, and NSAIDs. However, limitations prevent a widespread recommendation from being made due to study inconsistencies and a lack of direct comparison against other forms of analgesia such as opioids. For instance, there are a lack of studies directly measuring the reduction of analgesic burden after treatment with PRP for OA. Future research needs to be conducted directly comparing opioids with PRP and determining if patients using PRP require any additional analgesia. The recommendation from this integrative review is that PRP should be considered clinically in patients with mild to moderate OA as a reasonable alternative to traditional analgesics.

Appendix

Supporting material provided by the author is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJSJOPA/A290). This content has not been copyedited or verified.

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