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Platelet-rich plasma as a new treatment method in orthopedics

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Abstract

Introduction and purpose

Platelet-rich plasma (PRP) therapy represents a technology designed to enhance tissue repair by locally administering one's own bioactive agents, aiming to influence physiological processes like inflammation, angiogenesis, and extracellular matrix synthesis. Recently, the use of PRP therapy has become a subject of discussion in the orthopedic field. This review comprehensively examines the mechanisms, contemporary applications, clinical evidence, safety aspects, and potential future advancements of PRP in orthopedic treatment. Research has documented the efficacy of PRP injections in achieving full regeneration and enabling a comeback to competitive sports. PRP injections could serve as a viable alternative treatment for individuals with lateral tendonitis when compared to surgery. Further research investigating the impact of PRP on the bone healing process following a fracture is warranted.

Materials and methods

The methodology for conducting literature search involved utilizing medical subject headings terms to explore PubMed. Search terms included: "plasma-rich therapy", "tendinopathy", "injury" " articular cartilage ", "bone fracture "

Conclusions

Research at different evidence levels has shown that PRP is safe and has beneficial effects in

above uses. Due to the autologous nature of the therapy, side effects are minimal. In the majority of cases, PRP therapy alleviates pain sensations in both short- and long-term observations, facilitating a faster return to daily functionality. However, additional randomized, controlled clinical trials are anticipated to be conducted in the future. Progressing further necessitates the standardization of methods for preparing plasma and procedures for its application.

Keywords: plasma-rich therapy, orthopedics, Achilles tendinopathy, lateral elbow tendinosis bone fracture, cartilage injuries

Introduction

Platelet-rich plasma (PRP) is a blood derivative obtained from an individual's own blood, characterized by higher platelet concentrations than normal and containing growth factors associated with platelets. [1,2] Platelets come from the breakdown of megakaryocytic cells in the bone marrow and their value in whole blood ranges from 150,000 to 400,000 platelets/µl. [1,3] In PRP, the platelet count is escalated to three to six times greater than the initial baseline value observed in whole blood. [3] PRP is obtained through the centrifugation of an individual's own whole blood to isolate and amplify the concentration of platelets. [3] For over three decades PRP treatments have been employed across diverse medical conditions, sparking significant enthusiasm regarding the potential of autologous PRP within regenerative medicine. [1,2] The localized injection of concentrated platelets at injury sites has the potential to trigger tissue restoration by releasing numerous biologically active substances such as growth factors, cytokines, and adhesion proteins. This instigates a hemostatic cascade, production of new connective tissue and the process of revascularization. [2] Injuries to ligaments, tendons, and cartilage exhibit delayed healing due to their inadequate blood circulation and restricted inherent ability for regeneration. Platelet-rich plasma treatment becomes helpful in these conditions [3]

Objective of the work

This review aims is concentrate on the clinical utilization of platelet-rich plasma (PRP) therapy in managing assorted musculoskeletal pathologies.

Description of the state of knowledge

General Knowledge of PRP

Over the years, many platelet-rich platelet classification systems have emerged based on three main variables (i.e. platelets, leukocytes and fibrin content). [2] Considerations encompassed

aspects such as platelet activators, diverse platelet concentrations, and the purity of the preparation regarding the existence of erythrocytes, and leukocytes including neutrophils. Obtaining a consensus on the classification is a task for medical societies in the coming years.[2,4,5,6,7] In orthobiological applications, PRP is divided into three types: pure platelet-rich fibrin (P-PRF), leukocyte-rich PRP (LR-PRP), and leukocyte-poor PRP (LP-PRP) Leukocytes influence tissue regeneration and repair through immune and host defense mechanisms. [2,8] In the majority of documented instances, therapies involving platelet concentrates are collectively categorized as "PRP." [2] The difficulty in using PRP is the diversity of preparations and poor standardization of evidence-based guidelines. Clinical effectiveness is influenced by the content of platelets, purity and biological properties of added activators and preparations. There exist two methodologies for preparing PRP. The initial approach involves employing standard blood cell separators designed to process an entire unit of autologous blood. The second method uses gravity centrifugation techniques and devices. Centrifugation at high G force isolates the layers containing platelets and leukocytes from the blood unit. Different centrifugation times and strength result in differences in the efficiency, concentration and activity of isolated platelets. [9]

Clinical use of PRP

Tendinopathy

One of the most common problems in orthopedics are tendon disorders leading to impaired function and limitations in practicing sports and working ability. PRP is most often used as a regenerative stimulus in tendon tissue, which has a low potential for self-healing. PRP has demonstrated the ability to stimulate cell proliferation and enhance matrix synthesis within tenocytes, potentially supporting the regeneration and healing of tendons. Its autologous nature is due to the absence of some of the side effects commonly associated with traditional medications. It is administered via straightforward injections in conservative therapy and serves as a supplementary element during surgical interventions. [10]

Achilles Tendinopathy

Analyzing the results of individual studies, significant discrepancies appear regarding the use of PRP in the treatment of chronic Achilles tendon pathology. Deans et al. in 2012 showed statistically significant improvements in reduction of pain and other symptoms, return to sports and daily living activities, and overall quality of life. The study included 26 patients treated with PRP and standard rehabilitation, including weight bearing in a plaster boot, ultrasound therapy and exercises. [11] Two other randomized trials conducted at a similar

time showed no significant difference between PRP injection and saline injection in improving activity, reducing pain and ultrasonographic imaging in patients with chronic Achilles tendidopathy. [12,13] A multicenter, randomized clinical trial was conducted in patients with Chronic Midportion Achilles Tendinopathy over a 4-year period. 240 patients were intratendinous injected with PRP or a subcutaneous dry needle was inserted without entering the tendon as a placebo. 6 months after the start of treatment, the effects of therapy were assessed using the Victorian Institute of Sport Assessment-Achilles (VISA-A) score based on 8 questions covering 3 domains: pain, function and activity. Scores in the platelet-rich plasma group compared with the sham injection group were 54.4 versus 53.4 out of 100 points. Among side effects, injection site discomfort and swelling were common in patients receiving PRP, bruising was equally common in both groups. The obtained results do not indicate significant benefits in the use of PRP in the case of chronic tendinopathy of the central part of the Achilles tendon. [14] A review summarizing 11 randomized clinical trials examining the effect of platelet-rich plasma (PRP) on Achilles tendinopathy (AT) shows that AT patients in the PRP group had greater improvement in VISA-A score at week 6 after treatment initiation compared to placebo. After 3 and 6 months, no significant difference was observed between PRP and the control group. Furthermore, there were no differences between the two cohorts in terms of increased tendon thickness and pain relief in people with Achilles tendinopathy. [15] The most recent meta-analysis used a visual analogue scale [VAS] in addition to VISA-A to measure outcomes. At 12 weeks after treatment initiation, VAS scores and tendon thickness were significantly different in favor of PRP. It has been demonstrated that PRP injection is an effective treatment method, contributing to increased function and reduced discomfort in patients with chronic AT. Further randomized, controlled clinical trials are expected to be conducted. [16]

Shoulder Tendinopathy

Kwong et. al. conducted a randomized, controlled trial was conducted to compare the effectiveness of platelet-rich plasma (PRP) versus standard corticosteroid (CS) injections in relieving pain and improving function in patients diagnosed with rotator cuff tendinopathy and partial-thickness rotator cuff tears (PTRCT). At the three-month follow-up, patients administered with PRP demonstrated a more substantial enhancement in pain relief, as assessed using a visual analog scale (VAS) had a better outcome in American Shoulder and Elbow Surgeons (ASES) and Western Ontario Rotator Cuff Index (WORC) scores. At the extended follow-up period of 12 months, there wasn't a persistent advantage of PRP treatment

compared to CS in terms of sustained benefits. [17] Chen et al. conducted a meta-analysis of 18 clinical trials examining the effect of PRP in the treatment of rotator cuff abnormalities. Information pertaining to the Constant score, University of California, Los Angeles (UCLA) score, visual analog scale (VAS) for pain, retear rate, Simple Shoulder Test (SST), and American Shoulder and Elbow Surgeons (ASES) score was collected and analyzed across baseline, short-term, and long-term periods. Among patients treated with PRP who had multiple torn tendons, there were lower odds of experiencing retears. In short-term follow-up VAS results improved significantly. [18] Another large meta-analysis shows that the use of PRP resulted in significantly better results in terms of pain symptom control on the VAS scale in the medium-term (6 months) and long-term (12 months) follow-up. The clinical benefit of PRP has been documented to occur when the concentration of platelets ranges between 2.5 to 8.0 times higher than that found in whole blood. The group that received both PRP and sodium hyaluronate showed the most notable decrease in pain compared to other groups. Remarkably, although PRP exhibited a considerable advantage over the control group concerning pain symptoms, this effect does not consistently translate into improved shoulder function scores. The most frequently reported side effects among patients treated with PRP are temporary pain (up to 3 days). PRP could be regarded as a safe therapeutic option for managing rotator cuff tendinopathy. [19]

Patellar Tendinopathy

Patellar tendinopathy, commonly referred to as jumper's knee, typically manifests with anterior knee pain and tenderness at the lower end of the patella, resulting in substantial discomfort, particularly among individuals engaged in sports activities. The most recent major review studied the impact autologous platelet-rich plasma (PRP) injections in the treatment of patellar tendinopathy. Meta-analysis included eight clinical trials and assessed pain relief, as assessed using a visual analog scale (VAS), knee function or physical activities, as assessed by various questionnaires, and overall quality of life. The studies conducted did not reveal any disparities in pain alleviation and functional improvements between injections involving PRP and those without PRP. PRP injection demonstrated superiority in alleviating knee pain and enhancing functional activities, specifically in the short and medium terms, compared to no-injection treatment modalities such as ESWT (Extracorporeal Shock Wave Therapy). [20] Patellar tendinopathy commonly occurs in active individuals engaged in sports involving repetitive jumping, like volleyball, basketball, and soccer, with prevalence rates among elite

athletes reaching up to 14- 22%. Two studies documented the efficacy of PRP injections in attaining complete regeneration and enabling a return to competitive sports. [21,22]

Lateral Elbow Tendinosis

While surgical intervention is deemed dependable for lateral elbow tendinosis, local PRP injection therapy might be preferred due to its ability to circumvent the need for surgery. Kim et. al, based on a systematic review of the literature and meta-analysis, compared the treatment outcomes of patients treated with platelet-rich plasma injections or surgery for lateral tendinopathy of the elbow. Both types of treatment resulted in similar pain scores and functional outcomes among patients diagnosed with lateral elbow tendinosis. Hence, platelet-rich plasma injections could serve as a viable alternative treatment for patients reluctant to undergo surgery or deemed unsuitable candidates for surgical intervention. [23]

Low Back Pain

Low back pain is a prevalent and debilitating issue, representing the most frequent cause of disability among individuals aged 45 to 65 years. PRP has been shown to stimulate the metabolism of intervertebral disc cells in vitro. Local injection of PRP can be an effective method of relieving pain, disability and functional limitations. Meta-analysis findings indicate that PRP injection led to significantly enhanced pain relief, demonstrated by the analysis achieving over 50% pain relief at 3 months, along with improved patient satisfaction among individuals experiencing low back pain. Furthermore, an incorporated Randomized Controlled Trial (RCT) demonstrated that PRP injection led to sustained and greater reductions in pain, as indicated by VAS, and exhibited enhanced lumbar functional improvements at the 6-month mark compared to local anesthetic combined with corticosteroid use. [24] Levi et al. in a clinical trial performed a single treatment of intradiscal injection of PRP at one or multiple levels in 22 patient. In the 6-month observation following a single intradiscal PRP injection, 47% of patients reported at least a 50% improvement in pain perception on the VAS. Based on the current trial's findings, the hypothetical window for the potential beneficial effect on the disc appears to fall within the range of 2 to 6 months. [25]

Articular Cartilage Injury

Articular cartilage serves as a lubricant for joints, playing a pivotal role in facilitating smooth joint movements. Damaged cartilage releases metalloproteinases and inflammatory factors. Articular cartilage, once damaged, struggles to recover due to its lack of blood vessels and nerves, limiting nutrient supply from the joint fluid, and the inherent limited capacity of articular chondrocytes for effective repair at the injury site. The use of PRP can provide

significant benefits by promoting bone and cartilage healing by reducing inflammation, increasing angiogenesis, and stimulating chondrocyte proliferation and differentiation through the release of various growth factors and cytokines. Liang et al. included 13 clinical trials about PRP in repairing knee cartilage injury in the analysis. The majority of studies indicate a beneficial impact of PRP on cartilage injuries, leading to improved joint function. [26] In Tucker et al.'s randomized double-blinded trial involving 18 participants, findings revealed that individuals in the PRP group experienced a decrease in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores within 3 months from the baseline and sustained lower scores at 6 and 12 months. In contrast, patients who received a saline injection showcased minimal changes in WOMAC scores over the 12-month period. PRP influences the knee's local synovial environment by modifying the inflammatory conditions, reducing matrix degradation, and regulating angiogenic growth factors. [27] Xu et al showed that the combination of PRP with HA demonstrates greater effectiveness compared to PRP or HA alone in suppressing synovial inflammation, effectively enhancing pain relief and function, while reducing adverse reactions. This synergy operates through alterations in synovial tissue and cytokine composition. [28] In another study patients administered with PRP showcased more sustained symptom improvement for a duration of 12 months than HA, suggesting that these treatments might be the preferred option for long-term management. [29] According to Wu et al., the efficacy of PRP treatment is contingent upon the platelet concentration, with the optimal range being 1400-1800 x 10^9/L. Platelet concentrations that are either too high or too low can hinder the restoration of knee joint function. When PRP therapy is coupled with quadriceps training, it has the potential to expedite cartilage repair while decreasing inflammatory factors and matrix metalloproteinase levels. [30] However, standardized criteria or guidelines for its application are currently lacking.

Sports Injury

The favorable biological characteristics of PRP have led to its therapeutic application in sports medicine. Due to its biocompatibility and regenerative properties, percutaneous PRP injections are employed among athletes to address tendon and muscle injuries. Interventions in sports and musculoskeletal medicine target prompt, predictable tissue repair, expedited wound healing, and swift restoration of high mechanical performance and function in non-injured tissues. [31,32] A research conducted on 48 athletes, who sought treatment for diverse sports injuries at a sports medicine center, investigated the impact of PRP injections (single or multiple) by evaluating pain levels measured on a VAS scale. The study incorporated a

tailored rehabilitation program, and adherence to this regimen was evaluated using the Sports Injury Rehabilitation Adherence Scale (SIRAS). A one-year follow-up was carried out to evaluate player satisfaction and their return to play. Significant differences were observed between the pre-treatment and post-treatment VAS scores among all athletes. Athletes with lower-grade acute injuries requiring a single injection tended to return to sports activity sooner compared to those with chronic injuries needing multiple injections. PRP injections exhibit optimal effects in cases of sports injuries that do not respond adequately to conservative management. [33] A retrospective observational study assessed the efficacy of PRP therapy in 72 young athletes diagnosed with grade 2 meniscus tears and grade 2 anterior cruciate ligament (ACL) tears, confirmed through magnetic resonance imaging (MRI). Before and one month after PRP treatment, assessments were conducted on the Lysholm scale, pain intensity, and the ability to resume physical activities. The study demonstrated that patients exhibited enhanced subjective pain relief and improved Lysholm scores following PRP therapy. Simultaneously, 83.3% of patients successfully resumed sports and daily physical activities. This suggests that PRP therapy is a safe and straightforward method, proving effective in alleviating pain and enabling a return to sports activities among young recreational athletes. [34]

Bone Fracture Healing

Under normal healing circumstances, bone possesses the capability for complete regeneration. While fractures typically heal without complications, issues like delayed union or nonunion can still arise in around 10% of patients. Platelets contain growth factors and proteins promoting bone regeneration. Using platelet concentrates, known as platelet-rich plasma (PRP), locally appears promising for boosting fracture healing. The review of the eight clinical studies offers an overview of the utilization of PRP and its effects on enhancing fracture healing. [35] Two studies have demonstrated that PRP accelerates the healing process. [36,37] Most studies report a high rate of union in the control group, necessitating a substantial sample size to establish PRP's efficacy in enhancing fracture healing. [35]

Conclusion

Platelet-rich plasma therapy has been widely used in orthopedics. The safety of PRP injections is due to the fact that PRP comes from the patient's own blood. The popularity of platelet-rich plasma treatment is increasing due to its minimal side effects. Overall, the literature review indicates the potential positive impact of PRP on clinical outcomes. Incorporating PRP as an adjunctive therapy may offer advantages such as decreased pain,

enhanced tissue healing, and improved recovery. However, limited data availability, study discrepancies and inadequate methodological quality make it difficult to draw definitive conclusions.

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