

Platelet-Rich Plasma (PRP) in Orthopedic Sports Medicine

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Abstract

The use of platelet-rich plasma (PRP) injections in the treatment of musculoskeletal conditions has become more prevalent in recent years. Current literature has exhibited that PRP injections are relatively safe and can potentially accelerate or augment the soft tissue healing process. This review presents the most current literature update on the use of PRP in the treatment of rotator cuff tears, osteoarthritis of the knee, ulnar collateral ligament tears, lateral epicondylitis, hamstring injuries, and Achilles tendinopathy.

Platelet-rich plasma (PRP) is a refined product of autologous blood with a platelet concentration greater than that of whole blood. It is prepared via plasmapheresis utilizing a 2-stage centrifugation process and more than 40 commercially available systems are marketed to concentrate whole blood to PRP.¹ It is rich in biologic factors (growth factors, cytokines, proteins, cellular components) essential to the body's response to injury. For this reason, it was first used in oromaxillofacial surgery in the 1950s, but its effects on the musculoskeletal system have yet to be clearly elucidated.² However, this lack of clarity has not deterred its widespread use among orthopedic surgeons. In this review, we aim to delineate the current understanding of PRP and its proven effectiveness in the treatment of rotator cuff tears, knee osteoarthritis, ulnar collateral ligament (UCL) tears, lateral epicondylitis, hamstring injuries, and Achilles tendinopathy.

Rotator Cuff Tears

Rotator cuff tears are one of the most common etiologies for shoulder pain and disability. The

incidence continues to increase with the active aging population.³ Rotator cuff tears treated with arthroscopic repair have exhibited satisfactory pain relief and functional outcomes.⁴⁻⁷ Despite advances in fixation techniques, the quality and speed of tendon-to-bone healing remains unpredictable, with repaired tendons exhibiting inferior mechanical properties that are susceptible to re-tear.⁸⁻¹⁰

Numerous studies have investigated PRP application during arthroscopic rotator cuff repair (RCR) in an attempt to enhance and accelerate the repair process.¹¹⁻¹⁵ However, wide variability exists among protocols of how and when PRP is utilized to augment the repair. Warth and colleagues¹⁶ performed a meta-analysis of 11 Level I/II studies evaluating RCR with PRP augmentation. With regards to clinical outcome scores, they found no significant difference in pre- and postoperative American Shoulder and Elbow Surgeons (ASES), Constant, Disability of the Arm, Shoulder and Hand (DASH), or visual analog scale (VAS) pain scores between those patients with or without PRP augmentation. However, they did note a significant increase in Constant scores when PRP was delivered to the tendon-bone interface rather than over the surface of the repair site. There was no significant difference in structural outcomes (evaluated by magnetic resonance imaging [MRI] re-tear rates) between those RCRs with and without PRP augmentation, except in those tears >3 cm in anterior-posterior length using double-row technique, with the PRP group exhibiting a significantly decreased re-tear rate (25.9% vs 57.1%).¹⁶ Zhao and colleagues¹⁷ reported similar results in a meta-analysis of 8 randomized controlled trials, exhibiting no significant differences in clinical outcome scores or re-tear rates after RCR with and without PRP augmentation. Overall, most studies have failed to demonstrate a significant benefit with regards to re-tear rates or shoulder-specific outcomes with the addition of PRP during arthroscopic RCR.

Authors' Disclosure Statement: The authors report no actual or potential conflict of interest in relation to this article.

Knee Osteoarthritis

Osteoarthritis is the most common musculoskeletal disorder, with an estimated prevalence of 10% of the world's population age 60 years and older.¹⁸ The knee is commonly symptomatic, resulting in pain, disability, and significant healthcare costs. Novel biologic, nonoperative therapies, including intra-articular viscosupplementation and PRP injections, have been proposed to treat the early stages of osteoarthritis to provide symptomatic relief and delay surgical intervention.

A multitude of studies have been performed investigating the effects of PRP on knee osteoarthritis, revealing mixed results.¹⁹⁻²² Campbell and colleagues²³ published a 2015 systematic review of 3 overlapping meta-analyses comparing the outcomes of intra-articular injection of PRP vs control (hyaluronic acid [HA] or placebo) in 3278 knees. They reported a significant improvement in patient outcome scores for the PRP group when compared to control from 2 to 12 months after injection, but due to significant differences within the included studies, the ideal number of injections or time intervals between injections remains unclear. Meheux and colleagues²⁴ reported a 2016 systematic review including 6 studies (817 knees) comparing PRP and HA injections. They demonstrated significantly better improvements in Western Ontario and McMaster Universities Arthritis Index (WOMAC) outcome scores with PRP vs HA injections at 3 and 12 months postinjection. Similarly, Smith²⁵ conducted a Food and Drug Administration-sanctioned, randomized, double-blind, placebo-controlled clinical trial investigating the effects of intra-articular leukocyte-poor autologous conditioned plasma (ACP) in 30 patients. He reported an improvement in the ACP treatment group WOMAC scores by 78% compared to 7% improvement in the placebo group after 12 months. Despite the heterogeneity amongst studies, the majority of published data suggests better symptomatic relief in patients with early knee degenerative changes, and use of PRP may be considered in this population.

Ulnar Collateral Ligament Injuries

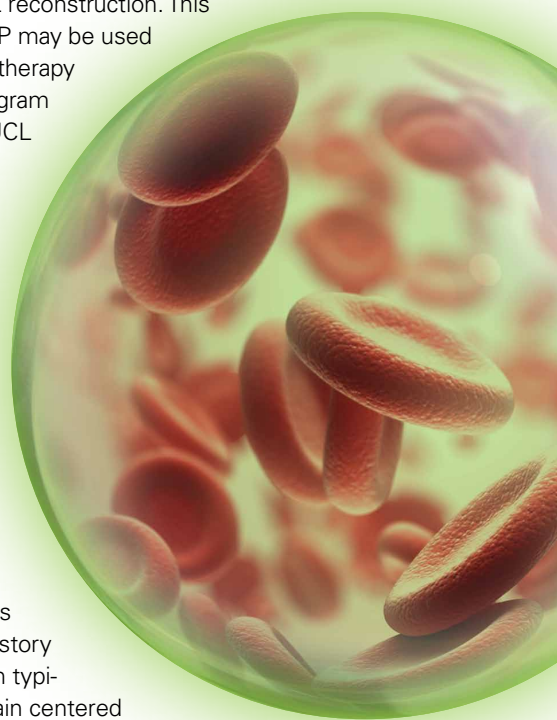
The anterior band of the UCL of the elbow provides stability to valgus stress. Overhead, high-velocity throwing athletes may cause repetitive injury to the UCL, resulting in partial or complete tears of the ligament. This may result in medial elbow pain, as well as decreased throwing velocity and accuracy. Athletes with complete UCL tears have few nonoperative treatment options and generally,

operative treatment with UCL reconstruction is recommended for those athletes desiring to return to sport. However, it remains unclear how to definitively treat athletes with partial UCL tears. Recently, there has been an interest in treating these injuries with PRP in conjunction with physical therapy to facilitate a more predictable outcome.

Podesta and colleagues²⁶ published a case series of 34 athletes with MRI-diagnosed partial UCL tears who underwent ultrasound-guided UCL injections and physical therapy. At an average follow-up of 70 weeks, they reported an average return to play (RTP) of 12 weeks, with significant improvements in Kerlan-Jobe Orthopaedic Clinic (KJOC) and DASH outcome scores, and decreased dynamic ulnohumeral joint widening to valgus stress on ultrasound. Most athletes (30/34) returned to their previous level of play, and 1 patient underwent subsequent UCL reconstruction. This study demonstrates that PRP may be used in conjunction with physical therapy and an interval throwing program for the treatment of partial UCL tears, but without a comparison control group, more studies are necessary to delineate the role of PRP in this population.

Lateral Elbow Epicondylitis

Lateral elbow epicondylitis, also known as "tennis elbow," is thought to be caused by repetitive wrist extension and is more likely to present in patients with various comorbidities such as rotator cuff pathology or a history of smoking.²⁷⁻²⁹ The condition typically presents as radiating pain centered about the lateral epicondyle. Annual incidence ranges from 0.34% to 3%, with the most recent large-scale, population-based study estimating that nearly 1 million individuals in the United States develop lateral elbow epicondylitis each year.³⁰ For the majority of patients, symptoms resolve after 6 to 12 months of various nonoperative or minimally invasive treatments.³¹⁻³³ Those who develop chronic symptoms (>12 months) may benefit from surgical intervention.³⁴ The use of PRP has become a contentious topic of debate in treating lateral epicondylitis. Its use and efficacy have been empirically



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examined and compared among more traditional treatments.³⁵⁻³⁷

In a small case-series of 6 patients, contrast-enhanced ultrasound imaging was utilized to demonstrate that PRP injection therapy may induce vascularization of the myotendinous junction of the common extensor tendon up to 6 months following injection.³⁸ These physiologic changes may precede observable clinical improvements. Brklijac and colleagues³⁹ prospectively followed 34 patients who had refractory symptoms despite conservative treatment and elected to undergo injection with PRP. At a mean follow-up of 26 weeks, 88.2% of the patients demonstrated improvements on their Oxford Elbow Score (OES). While potentially promising, case series lack large sample sizes, longitudinal analysis, and adequate control groups for comparative analyses of treatments, thereby increasing the likelihood of unintended selection bias.

Randomized controlled trials have demonstrated no difference between PRP and corticosteroid (CS) injection treatments in the short term for symptomatic lateral elbow epicondylitis. At 15 days, 1 month, and 6 months postinjection, no significant difference was found between PRP and CS injections in dynamometer strength measurements nor patient outcome scores (VAS, DASH, OES, and Mayo Clinic Performance Index for Elbow [MMCPPIE]).^{40,41} In fact, multiple randomized controlled trials have demonstrated PRP to be less effective at 1 and 3 months compared to CS injections, as assessed by the Patient Rated Tennis-Elbow Evaluation (PRTEE) questionnaire, VAS, MMCPPIE, and Nirschl scores.^{42,43} One mid-term, multi-center randomized controlled trial published by Mishra and colleagues⁴⁴ compared PRP injections to an active control group, demonstrating a significant improvement in VAS pain scores at 24 weeks, but no difference in the PRTEE outcome. The available evidence indicates PRP injection therapy remains limited in utility for treatment of lateral epicondylitis, particularly in the short term when compared to CS injections. In the midterm to long term, PRP therapy may provide some benefit, but ultimately, well-designed prospective randomized controlled trials are needed to delineate the effects of PRP versus the natural course of tendon healing and symptom resolution.

Hamstring Injuries

Acute hamstring injuries are common across all levels and types of sport, particularly those in which sprinting or running is involved. While there is no consensus within the literature on how RTP after hamstring injury should be managed or defined, most injuries seem to resolve around 3 to 6 weeks.⁴⁵ The proximal myotendinous junction of the long head of the biceps femoris and semitendinosus are commonly associated with significant pain and edema after acute hamstring injury.⁴⁶ The amount of edema resulting from grade 1 and 2 hamstring injuries has been found to correlate (minimally) with time to RTP in elite athletes.⁴⁷ PRP injection near the proximal myotendinous hamstring origin has been theorized to help speed the recovery process after acute hamstring injury. To date, the literature demonstrates mixed and limited benefit of PRP injection therapy for acute hamstring injury.

Few studies have shown improvements of PRP therapy over typical nonoperative management (rest, physical therapy, nonsteroidal anti-inflammatory drugs) in acute hamstring injury, but the results must be interpreted carefully.^{48,49} Wetzell and colleagues⁴⁸ retrospectively reviewed 17 patients with acute hamstring injury, 12 of whom failed typical management and received PRP injection at the hamstring origin. This group demonstrated significant improvements in their VAS and Nirschl scores at follow-up, whereas the 5 patients who did not receive the injection did not. However, this study exhibited significant limitations inherent to a retrospective review with a small sample size. Hamid and colleagues⁴⁹ conducted a randomized controlled trial of 24 athletes with diagnosed grade 2a acute hamstring injuries, comparing autologous PRP therapy combined with a rehabilitation program versus rehabilitation program alone. RTP, changes in pain severity (Brief Pain Injury-Short Form [BPI-SF] questions 2-6), and pain interference (BPI-SF questions 9A-9G) scores over time were examined. Athletes in the PRP group exhibited no difference in outcomes scores, but returned to play sooner than controls (26.7 vs 42.5 days).

Mejia and Bradley⁵⁰ have reported their experience in treating 12 National Football League (NFL) players with acute MRI grade 1 or 2 hamstring injuries with a series of PRP injections at the site of injury. They found a 1-game difference in earlier RTP when compared to the predicted RTP based on MRI grading. Similarly, Hamid and colleagues⁴⁹ performed a randomized control trial published in

2014, reporting an earlier RTP (26.7 vs 42.5 days) when comparing single PRP injection vs rehabilitation alone in 28 patients diagnosed with acute ultrasound grade 2 hamstring injuries. On the contrary, a small case-control study of NFL players and a retrospective cohort study of athletes with severe hamstring injuries demonstrated no difference in RTP when PRP injected patients were compared with controls.^{51,52} Larger randomized controlled trials have demonstrated comparable results, including a study of 90 professional athletes in whom a single PRP injection did not decrease RTP or lessen the risk of re-injury at 2 and 6 months.⁵³ In another large multicenter randomized controlled trial examining 80 competitive and recreational athletes, PRP did not accelerate RTP, lessen the risk of 2-month or 1-year re-injury rate, or improve secondary measures of MRI parameters, subjective patient satisfaction, or the hamstring outcome score.⁵⁴ Although further study is warranted, available evidence suggests limited utility of PRP injection in the treatment of acute hamstring injuries.

Achilles Tendinopathy

Noninsertional Achilles tendinopathy is a common source of pain for both recreational and competitive athletes. Typically thought of as an overuse syndrome, Achilles tendinopathy may result in significant pain and swelling, often at the site of its tenuous blood supply, approximately 2 to 7 cm proximal to its insertion.⁵⁵ Conservative management frequently begins with rest, activity/shoe modification, physical therapy, and eccentric loading exercises.⁵⁶ For those whom conservative management has failed to reduce symptoms after 6 months, more invasive treatment options may be considered. Peritendinous PRP injection has become an alternative approach in treating Achilles tendinopathy refractory to conservative treatment.

In the few randomized controlled trials published, the data demonstrates no significant improvements in clinical outcomes from PRP injection for Achilles tendinopathy. Kearney and colleagues⁵⁷ conducted a pilot study of 20 patients randomized into PRP injection or eccentric loading program for mid-substance Achilles tendinopathy, in which Victorian Institute of Sports Assessment (VISA-A), EuroQol 5 dimensions questionnaire (EQ-5D), and complications associated with the injection were recorded at 6 weeks, 3 months, and 6 months. Although this was a pilot study with a small sample size, no significant difference was found between groups across these time periods. Similarly, de

Vos and colleagues^{58,59} conducted a double-blind randomized controlled trial of 54 patients with chronic mid-substance Achilles tendinopathy and randomized them into eccentric exercise therapy with either a PRP injection or a saline injected placebo groups. VISA-A scores were recorded and imaging parameters assessing tendon structure by ultrasonographic tissue characterization and color Doppler ultrasonography were taken with follow-up at 6, 12, and 24 weeks. VISA-A scores improved significantly in both groups after 24 weeks, but the difference was not statistically significant between groups. In addition, tendon structure and neovascularization (exhibited by color Doppler ultrasonography) improved in both groups, with no significant difference between groups. The current literature does not support the use of PRP in treatment of Achilles tendinopathy, as it has failed to reveal additional benefits over conventional treatment alone. Future prospective, well-designed randomized controlled trials with large sample sizes will need to be conducted to ultimately conclude whether or not PRP deserves a role in the treatment of Achilles tendinopathy.

Summary

In theory, the use of PRP within orthopedic surgery makes a great deal of sense to accelerate and augment the healing process of the aforementioned musculoskeletal injuries. However, the vast majority of published literature is Level III and IV evidence. Future research may provide the missing critical information of optimal growth factor, platelet, and leukocyte concentrations necessary for the desired effect, as well as the appropriate delivery method and timing of PRP application in different target tissues. Evidence-based guidelines to direct the use of PRP will benefit from more homogeneous, repeatable, and randomized controlled trials.

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This paper will be judged for the Resident Writer's Award.