Editorial Commentary: Platelet-Rich Plasma Shows Promise for Improving Shoulder Tendinopathy

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Abstract: Platelet-rich plasma (PRP) injections continue to be used at increasing rates to treat common musculoskeletal conditions. PRP has a low-risk profile and emerging in vitro evidence to support its positive effects on soft-tissue healing. PRP has been shown to be of benefit for knee osteoarthritis, but less has been published regarding the shoulder. PRP delivers a high concentration of growth factors, cytokines, and other important inflammatory modulators. Its use is appealing for treating partial-thickness rotator cuff tears, subacromial bursitis, and rotator cuff tendinopathy since rotator cuff tendons often have poor healing capacity due to intrinsic degeneration. PRP has been shown to increase cell proliferation and matrix synthesis in tenocytes, which may aid tendon regeneration and healing. Adult tendons also contain a small amount of tendon progenitor cells, which can be induced to an active state by PRP. In addition, PRP is an autologous biologic agent and easy to acquire and administer in an outpatient clinical setting. Clinical studies continue to lag and are often heterogenous in quality and in results. PRP can vary widely based on multiple intrinsic and extrinsic factors, including patient age, sex, activity level, centrifugation speed, and number of centrifugation cycles. Thus, quality research methods should include reporting using the PAW (platelets/activation/white blood cells) system. Clinicians should remain cautiously optimistic about the future role of PRP injections in the shoulder.

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Platelet-rich plasma (PRP) is an attractive biologic agent because of its ease of acquisition and administration in an outpatient clinical setting. Unfortunately, high-quality research to elucidate appropriate indications for PRP is generally lacking, especially for most shoulder pathologies. The authors of "Subacromial Platelet-Rich Plasma Injections Decrease Pain and Improve Functional Outcomes in Patients With Refractory Rotator Cuff Tendinopathy,"[1] Rossi, Piuzzi, Giunta, Tanoira, Brandariz, Pasqualini, and Ranalletta, should be commended for a well-performed study that is a positive step in clarifying the role of PRP in the management of a common shoulder pathology.

In their prospective cohort study, 50 patients (mean age 37.3 years) with rotator cuff tendinopathy confirmed by magnetic resonance imaging (MRI) were offered a PRP injection to the subacromial space after no response to 3 months of conservative measures and a subacromial corticosteroid injection within 6 months. All PRP formulations were leukocyte-rich, and each sample was analyzed for the quality of PRP contents. The visual analog scale, American Shoulder and Elbow Surgery, and Constant scores each showed statistical improvement ($P < .001$) with 80% and 86% of patients achieving substantial clinical benefit in the American Shoulder and Elbow Surgery and Constant scores, respectively. In addition, 86% of patients with preinjection insomnia reported resolution of these symptoms by 6-month follow-up. Return to sports was achieved in 84% of patients, with 78% returning to previous level of play. Finally, while all PRP was leukocyte rich and met a minimum level of concentration (PA-4α),[2] the authors did not find a correlation between the improvement in functional scores and the final concentration of platelets, leukocytes, or neutrophils.

PRP has rapidly gained popularity due to its simple acquisition process, ease of administration, low-risk profile, and emerging in vitro evidence to support its positive effects on soft tissue healing. Its ability to deliver a high concentration of growth factors and

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cytokines is especially appealing when treating rotator cuff pathology, since the rotator cuff tendons often demonstrate poor healing capacity due to intrinsic degeneration. Furthermore, PRP has been shown to increase cell proliferation and matrix synthesis in tenocytes, which may aid tendon regeneration and healing.[3,4] Adult tendons also contain a small amount of tendon progenitor cells, which can be induced to an active state by PRP.[5,6] For these reasons, PRP has great promise for treating common shoulder pathologies, including partial-thickness rotator cuff tears, subacromial bursitis, and rotator cuff tendinopathy. However, clinical results have been lacking with generally mixed results. For example, Kesikburun et al.[7] performed a double-blinded randomized controlled trial in 40 patients with chronic rotator cuff tendinopathy. Patients were given either a PRP or a normal saline injection followed by physical therapy. There was no difference between the 2 groups in functional outcome or pain scores at any point within 1 year of follow-up.

In contrast, the current study is a positive advocate for the use of PRP with physical therapy in the management of rotator cuff tendinopathy. There are multiple important strengths of this study that should be modeled in future studies. The authors had strict inclusion and exclusion criteria, allowing for a fairly homogenous group of patients. Most importantly, the content of each PRP sample was analyzed and classified by the PAW system (platelets/activation/white blood cells).[2] This step is paramount for all studies investigating PRP because it ensures that each patient receives a similar PRP injection, and it ensures repeatability and appropriate comparison for future studies. This is important since the content of PRP can vary widely based on multiple intrinsic and extrinsic factors, including patient age, sex, activity level, centrifugation speed, and number of centrifugation cycles.[8-11]

There are also a few important questions that are left unanswered and merit further investigation. Perhaps most importantly, what is the mechanism for PRP's effectiveness in the current study? Does the PRP injection actually stimulate healing in the rotator cuff tendon? Does the PRP injection relieve pain by simply altering the inflammatory milieu of the subacromial space with or without changing the quality of the rotator cuff tendon? The latter is certainly possible since leukocyte-rich formulas, like the one used in the current study, tend to create a heightened inflammatory response. The lack of MRI is an appropriately stated limitation. Including MRI follow-up is a logical building block for future studies to better understand the mechanism of improvement in these patients. Another important question left unanswered is how long can a patient expect durable results from the PRP injection. Longer follow-up beyond 1 year is needed, and I hope the current authors will continue to follow this cohort to help provide this answer. Lastly, 10 patients (20% of all patients) did not improve after the first injection. Of these 10 patients, only 3 patients improved with a second injection. While an 80% initial success rate is still very encouraging, a larger cohort is needed to confirm these results and to decipher potential risk factors for why some patients may not respond to an initial PRP injection.

In a world of mixed clinical results following a PRP injection, I view the current study as a win for PRP. Certainly, more studies are needed to make definitive conclusions on the usefulness of PRP in treating rotator cuff tendinopathy and other common shoulder pathologies. Until then, I firmly believe that clinicians should remain cautiously optimistic about the future role of PRP injections in the management of common musculoskeletal conditions.

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