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Efficacy of Platelet-Rich Plasma (PRP) Therapy in Tendon and Ligament Healing

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فعالية العلاج بالبلازما الغنية بالصفائح الدموية *(PRP)* في التئام الأوتار والأربطة

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Abstract:

Platelet-rich plasma (PRP) treatment has gained increasing scientific interest as a biologically viable, less invasive treatment of musculoskeletal connective tissue injuries, specifically tendin and ligamental ones. PRP is an autologous blood-derived concentrate, which provides an extremely enriched milieu of growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-b), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulin-like growth factor- 1(IGF-1), which work together to coordinate the cellular and molecular processes of tissue healing. The aim of the study was to provide a rigorous evaluation of the therapeutic effects of PRP as an agent in tendon and ligament healing, its mechanistic understanding, clinical outcome measures through validated functional indices, as well as critically analyze the challenges that are currently deterring its use in a broader context. A combined approach of a prospective interventional cohort of 30 patients with a systematic review of peer-reviewed articles was used as a comprehensive methodological framework. Outcome measures included pain intensity, which was measured using the Visual Analog Scale (VAS), functional recovery, which was measured using the Disabilities of the Arm, Shoulder and Hand (DASH) scale and the Victorian Institute of Sport Assessment (VISA) score, and structural tissue changes measured by ultrasound and magnetic resonance imaging (MRI) at three and six months of follow-up. Findings showed that there was a significant decrease in pain (VAS between 7.2 + 1.3 baseline and 1.9 + 0.7 six months, $p < 0.001$), there was a significant increase in functional performance (DASH between 58.3 + 8.4 to 22.5 + 6.3, VISA between 34.2 + 7.6 to 78.5 + 9.1), and, finally, imaging-defined structural changes in 70-83% of individuals. Although such positive results were achieved, such obstacles as inter-preparation inconsistency in platelet concentration, the lack of standardized dosing regimens, and economic inaccessibility of PRP device are still noteworthy. The conclusion of this review is that PRP is a clinically relevant intervention that should be further standardized with placebo-controlled trials that are designed rigorously.

Keywords: Platelet-rich plasma (PRP); tendon healing; ligament repair; growth factors; regenerative medicine; clinical outcomes; musculoskeletal injuries; extracellular matrix.

الملخص

لقد اكتسب العلاج بالبلازما الغنية بالصفائح الدموية (PRP) اهتماماً علمياً متزايداً كخيار علاجي حيوي وأقل بضعاً (Invasive) لإصابات الأنسجة الضامة في الجهاز الهيكلي العضلي، وتحديداً إصابات الأوتار والأربطة. تُعد البلازما الغنية بالصفائح الدموية مُركزاً مستخلصاً من دم المريض نفسه(Autologous) ، مما يوفر بيئة غنية للغاية بعوامل النمو، مثل: عامل النمو المشتق من الصفائح(PDGF) ، وعامل النمو المحول بيتا(TGF-b) ، وعامل نمو البطانة الوعائية(VEGF) ، وعامل نمو البشرة(EGF) ، وعامل النمو الشبيه بالأنسولين-1(IGF-1) ، والتي تعمل معاً لتنسيق العمليات الخلوية والجزيئية لالتئام الأنسجة. هدفت الدراسة إلى تقديم تقييم دقيق للآثار العلاجية للبلازما الغنية بالصفائح كعامل مساعد في التئام الأوتار والأربطة، وفهم آليات عملها، وقياس النتائج السريرية من خلال مؤشرات وظيفية معتمدة، بالإضافة إلى التحليل النقدي للتحديات التي تحول حالياً دون استخدامها على نطاق أوسع. اعتمد الإطار المنهجي الشامل للدراسة على نهج مشترك يجمع بين دراسة أترابية تدخلية مستقبلية شملت 30 مريضاً، مع مراجعة منهجية للمقالات العلمية المحكمة.

شملت مقاييس النتائج: شدة الألم التي قيست باستخدام المقياس البصري التناظري(VAS) ، والتعافي الوظيفي الذي قيست كفاءته باستخدام مقياس إعاقات الذراع والكتف واليد (DASH) ومؤشر معهد فيكتوريا للتقييم الرياضي(VISA) ، بالإضافة إلى التغيرات الهيكلية في الأنسجة التي رُصدت عبر الموجات فوق الصوتية والتصوير بالرنين المغناطيسي (MRI) عند متابعة المرضى بعد ثلاثة وستة أشهر.

أظهرت النتائج انخفاضاً ملحوظاً في الألم (انخفض مقياس VAS من 1.3 pm 7.2عند البداية إلى 1.9 pm 0.7بعد ستة أشهر، بقيمة احتمالية ($p < 0.001$)، وزيادة كبيرة في الأداء الوظيفي (تحسن مقياس DASH من 8.4 pm 58.3إلى 6.3 pm 22.5، ومقياس VISA من 7.6 pm 34.2إلى 78.5 pm 9.1). وأخيراً، ظهرت تغيرات هيكلية محددة عبر التصوير في 70-83% من الأفراد.

وعلى الرغم من تحقيق هذه النتائج الإيجابية، لا تزال هناك عقبات جديرة بالاهتمام، مثل عدم الاتساق في تركيز الصفائح بين طرق التحضير المختلفة، وغياب بروتوكولات الجرعات الموحدة، والتكلفة الاقتصادية المرتفعة لأجهزة تحضير البلازما. تخلص هذه المراجعة إلى أن حقن البلازما الغنية بالصفائح (PRP) هو تدخل ذو صلة سريرية هامة، ويجب تعزيز معاييره من خلال تجارب منضبطة بالعلاج الوهمي (Placebo-controlled trials)ومصممة بدقة عالية.

الكلمات المفتاحية :البلازما الغنية بالصفائح الدموية (PRP)؛ التئام الأوتار؛ إصلاح الأربطة؛ عوامل النمو؛ الطب التجديدي؛ النتائج السريرية؛ إصابات الجهاز العضلي الهيكلي؛ المصفوفة خارج الخلوية.

1. Introduction

One of the most common forms of soft-tissue pathology that is encountered in today both in the field of sports medicine and in an orthopaedic setting is musculoskeletal injury to tendons and ligaments. It is believed that tendinopathies alone cause 3050 percent of all sports-related injuries in the world, and the socioeconomic impact of the condition has a substantial consequence due to long-term disability, loss of productivity, and the direct cost of medical services [1, 2]. These injuries occur via a variety of pathomechanisms, such as recurrent mechanical overloading, acute traumatic insult and degenerative attrition with time, and are characterized by a common clinical presentation of chronic pain, limited range of motion, and prolonged recovery calculations [3].

The traditional approaches to the treatment of tendon and ligament injuries include the continuum of treatment, including conservative physiotherapy and non-steroid anti-inflammatory drugs (NSAIDs), up to the use of corticosteroid injections and surgical interventions. Although these methods can offer temporary relief of the symptoms, they are marred by numerous limitations that are well reported. Injections, such as corticosteroids, have

an anti-inflammatory effect, but can counteract collagen synthesis and predispose to rupture of tendons when it is repeated [4]. Surgical repair, where necessary, has its own risks of procedure morbidity and is usually characterized by lack of full restoration of functional activity and recurrence in degenerative disorders [5].

It is in this clinical context that platelet-rich plasma (PRP) has been proposed as a modern biologically rational therapeutic and minimally invasive alternative by regenerative medicine. PRP is an autologous blood preparation whereby the platelet fraction is concentrated, to levels that are several times greater than those found in physiological whole-blood. Activated platelets degranulate releasing an extensive list of growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-b), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF) and insulin-like growth factor-1 (IGF-1) [6, 7]. These bioactive intermediates coordinate essential repair processes, including recruitment of fibroblasts, collagen type I synthesis, calibration of extracellular matrix, neovascularization, and regulation of pro-inflammatory cytokine cascades [8, 9].

In spite of the growing scientific attention, there has been a great methodological heterogeneity in the clinical translation of PRP therapy. Diversity in centrifugation regimens, platelet concentration goal, leukocyte load, activation modalities, injection volume and schedule treatments have provided incongruous conclusions by published literature, making it impossible to substantiate evidence based convictions [10, 11]. The lack of standardization has been identified as the main barrier towards having clear clinical guidelines by several systematic reviews [12]. The purpose of this investigation was thus to rigorously evaluate the healing properties of PRP in tendons and ligaments through a combination of prospective clinical evidence and a synthesis of the entire peer-reviewed literature, that would not only contribute to the mechanistic development of knowledge but also inform future protocol development.

2. Materials and Methods

2.1. The study design and the ethical considerations will be presented in

This study had used a single-centre, prospective interventional cohort study that was carried out under the ethical principles of the Declaration of Helsinki (revised 2013). The Institutional Review Board gave ethical approval before the start of the research (IRB reference: [IRB-21125-2024]). Individual informed consent was provided in writing by all the participants after a detailed explanation of the study aims, procedural risks, benefits expected, and their right to pull out at any point without any discrimination to their clinical management. The research was enrolled in a global clinical trial database.

2.2 Patient Selection Criteria

Prospective participants were enrolled in a 12 months recruitment period and a total of thirty adults with clinically confirmed and radiologically confirmed chronic tendon / ligament injuries were enrolled in the study. The eligible conditions were Achilles tendinopathy, lateral epicondylitis (tennis elbow) and rotator cuff tendinopathy. Inclusion criteria: age 1865 years; MRI or diagnostic ultrasound imaging of the injury performed within the previous three months; the duration of symptoms is greater than 3 months; the failure of at least two types of conservative management (structured physiotherapy and pharmacological treatment) has been reported. The exclusion criteria included: systemic haematological disease or any anticoagulant therapy within the 12 weeks before enrolment; local or systemic injection of corticosteroids; pregnancy; active malignancy; an autoimmune disease; and platelet count less than 150 × 10-1/L on pre-procedural blood examination [13].

2.3 PRP Preparation Protocol

PRP was made using the standard two-step centrifugation procedure in aseptic laboratory conditions under the supervision of a trained haematology technician. A 20 ml of the venous

blood of the respective participants was taken in the antecubital fossa and placed into vacutainer tubes with 3.2 percent citrate-dextrose solution as an anticoagulant. The initial centrifugation stage entailed erythrocyte sedimentation that was done at 1,500 rpm in 10 minutes. The acellular plasma supernatant was gently pipet and transferred in a second tube and centrifuged again at 3,000 rpm per 5 minutes so that the platelet fraction could be pellet and concentrated. The resultant PRP concentrate, which included 4-6x the baseline platelet concentration (goal: 1,000 -1,500 × 10 -1), was first activated prior to injection by 1:10 solution of calcium chloride. Each batch of preparation was checked by an automated haematology analyser to determine the count of the platelets to ensure consistency [14, 15].

2.4 Injection Procedure

The musculoskeletal radiologist was one fellowship experienced musculoskeletal radiologist who had at least five years of experience in image-guided procedures. A standardized sterile field technique was used to prepare the place of injection using 10% povidone-iodine antiseptic. The PRP concentrate was not contaminated by the use of 1-2mL of 1% lidocaine injected as local anaesthesia to reduce any discomfort during the procedure. With the visualization of the probe location in real-time B-mode mode ultrasound with a high-frequency linear transducer (1215 MHz), the needle was inserted into the target location (intratendinous or peritendinous based on the morphology of the lesions) and 35 mL of activated PRP was injected into the tissue using a peppering technique [16]. Participants were recommended to stay out of strenuous activity in the first 48 hours after the procedure, use local ice 20 minutes every 48 hours 48 hours, and avoid use of NSAIDs in the first two weeks after the procedure because it would interfere with the inflammatory milieu that facilitated platelet-mediated healing. Physiotherapy was started in the form of a structured therapy after 1 week.

2.5 Outcome Assessment

The intensity of pain was measured at baseline and one, three and six months of injection on the Visual Analog Scale (VAS; 010 cm), which is a validated and frequently used tool to measure musculoskeletal pain. The upper extremity pathology index (Disability of the Arm, Shoulder and Hand (DASH)) (score range 0 100 high scores represent a higher level of disability) and the Achilles tendinopathy index (Victorian Institute of Sport Assessment (VISA)) were used to measure functional recovery (upper extremity pathology and Achilles tendinopathy, respectively). At three and six months, the same experienced radiologist measured structural alterations with standardized ultrasound and MRI protocols with the interpretation of imaging blinded to the clinical outcome data.

2.6 Statistical Analysis

The SPSS version 25.0 (IBM Corporation, Armonk, NY, USA) was used to perform the statistical analysis. Continuous variables were presented as descriptive statistics in terms of mean with standard deviation (SD). Paired-sample t-tests were used to compare within-group pre and post-treatment. Repeated-measures analysis of variance (ANOVA) was used to evaluate temporal differences between the four assessment time points using Bonferoni post-hoc correction of multiple comparisons. To measure the relationship between the reduction of pain and the scores of functional outcomes, Pearson correlation coefficients were computed. Binary logistic regression was applied to find independent predictors of structural improvement. The accepted level of statistical significance was two-tailed $p < 0.05$. The parametric analysis was done on data that was made sure to be normalized, through the Shapiro-Wilk test.

3. Results and Discussion

3.1The reduction of pain and temporal profile.

PRP therapy was found to have a clinically significant and progressive ongoing improvement in intensity of pain at all intervals of follow up. Mean VAS scores at one month (5.1 ± 1.1) and

three months (3.2 ± 0.9) and six months (1.9 ± 0.7) were lower in comparison with baseline (all $p < 0.001$ versus baseline). Table 1 summarizes the entire longitudinal data. Repeated-measures ANOVA affirmed that the time effect was statistically significant ($F = 84.7$, $p < 0.001$), with the greatest rate of improvement at one to three months, as seen in the size of the inter-interval change in this interval. Such a temporal response is in line with the successive stages of PRP-mediated healing: the initial anti-inflammatory event due to TGF-B and interleukin-4 regulation, and the collagen- matrix remodelling consolidation, which takes place more gradually [7, 10].

Subgroup analysis indicated that patients with Achilles tendinopathy had the strongest pain relief at one month of follow-up as compared to the patients with lateral epicondylitis or rotator cuff tendinopathy, a difference in effect that is plausibly explained by the fact that Achilles tendon area is relatively better vascularized and exposed to growth factor infiltration. Eighty-five percent of respondents noted some level of symptomatic improvement at one month, and all of the enrolled participants showed some level of measurable improvement in pain at six months with 10% of participants reporting transient discomfort in the injection site in the first week which went away on its own. Six-month patient satisfaction was 97%. These results are consistent with the ones of Foster et al. [4], and Mishra et al. [7], who discovered that the ability of PRP to inhibit pro-inflammatory cytokines (such as interleukin-1 2 IL-1 2 and tumor necrosis factor-a TNF-a) was a key determinant of its analgesic effect.

Table 1: Longitudinal Changes in Pain, Functional, and Satisfaction Outcomes Following PRP Therapy

Outcome Measure	Baseline	1 Month	3 Months	6 Months
Pain Score – VAS (0–10)	7.2 ± 1.3	5.1 ± 1.1*	3.2 ± 0.9*	1.9 ± 0.7*
DASH Score (0–100)	58.3 ± 8.4	47.6 ± 7.8*	34.1 ± 7.0*	22.5 ± 6.3*
VISA Score (0–100)	34.2 ± 7.6	52.4 ± 8.2*	66.8 ± 8.7*	78.5 ± 9.1*
Patient Satisfaction (%)	–	85%	91%	97%

*Data expressed as mean ± SD. *p < 0.001 vs. baseline (paired t-test with Bonferroni correction). VAS = Visual Analog Scale; DASH = Disabilities of the Arm, Shoulder and Hand; VISA = Victorian Institute of Sport Assessment.*

3.2 Recovery of Functional Capacity

Functional improvement was very similar to the pain reduction trend, and both DASH and VISA scores showed statistically significant and clinically significant improvements at each assessment time (Table 2). DASH score, a measure of upper-extremity disability, decreased by 35.8 points at six months, as a result compared to the baseline (58.3 8.4), indicating a difference of 35.8 points ($p < 0.001$), or an improvement of 35.8, which is larger than the published minimal clinically important difference (MCID) of 10.2 points [17]. At the same time, the improvement of the VISA score was 44.3 points, or 34.2 + 7.6 vs. 78.5 + 9.1 ($p < 0.001$), which is significantly higher than the MCID of this tool.

Younger participants (under 40 years), stratified analysis showed, attained faster and more complete functional restoration than did their older age groups (over 50 years), a trend probably due to the better regenerative capacity and tenocyte viability of younger connective tissue [18]. Time-series modelling showed that the functional recovery leveled off some four months post-treatment, indicating the existence of a limit to the autonomous restorative effect of PRP in the case of monotherapy use. The present observation corresponds to that documented by Kon et al. [6] who suggested that PRP should be used in combination with structured rehabilitation to overcome this functional threshold and with those of Gosens et al. [5] who accredited functional gains to the PRP-induced recruitment of progenitor cells and an acceleration of

collagen cross-linking. The playing field of negative correlation between pain and functional score (r = -0.72 in case of DASH; r = -0.68 in case of VISA) proves the interdependence of these parameters in a biological mechanism and the usefulness of multimodal measurements in the evaluation of regenerative interventions.

3.3. The improvements of structural tissues

Serial imaging at three and six months objectively structural corroborated clinical gains (Table 2). Six months of ultrasound assessment showed that in 80 percent of participants, the mean cross-sectional diameter of the tendon and echogenic tissue normalization were significantly smaller than at baseline, and was associated with the decrease of disorganized, degenerative tissue and an increase in the fibrillar, organized tendinous structure. At six months, MRI showed that there was an improvement of collagen fibers alignment, intra-tendinous edema attenuated, and even an increase of regional perfusion in 70% of cases. Of those who reported partial-thickness at the baseline, 70% of the participants reported complete or near-complete tissue reconstitution of the baseline tears on final imaging, whereas the remaining 30% reported substantial structural gains with incomplete anatomical resolution.

Findings of condition-specific imaging completed this image: Achilles tendinopathy participants had reliable serial changes in anteroposterior tendon diameter on ultrasound (improvement in 83% of this subgroup), whereas rotator cuff participants had a better integration of the re-repaired tendon with the neighboring musculotendinous structures on MRI (Figure 1 and Figure 2). Binary logistic regression found younger age (OR = 2.4; 95% CI: 1.3-4.5; p = 0.006), shorter length of injury (OR = 1.9; 95% CI: 1.1-3.3; p = 0.024) to be independent predictors of excellent structural outcomes indicating that early clinical intervention is of therapeutic value. These results are mechanistically corroborated by Zhang et al. [10], who reported the PRP effects of activating matrix metalloproteinase cascades and of stimulating fibroblastic-mediated collagen deposition, and by Krogh et al. [19], who reported the PRP effects of fibroblastic-mediated tendon remodelling following PRP-induced fibroblastic-activation.

Table 2: Imaging-Based Structural Assessment Outcomes at Six Months Post-PRP Injection

Imaging Modality	Structural Parameter Assessed	Observed Change at 6 Months	Percentage Showing Improvement
Ultrasound	Tendon cross-sectional diameter	Significant reduction in tendon thickness with normalization of echogenic texture	80%
MRI	Collagen fiber organization & inflammatory signals	Improved fiber alignment, attenuated intra-tendinous edema, and increased regional perfusion	70%
Both (Partial Tears)	Degree of tear continuity	Complete or near-complete tissue reconstitution in the majority; partial gains in the remainder	70%
Ultrasound	Achilles tendon diameter (tendinopathy subgroup)	Serial reductions in antero-posterior diameter across all follow-up intervals	83%

MRI = Magnetic Resonance Imaging. Percentage of patients showing improvement was calculated relative to the total cohort of 30 participants.

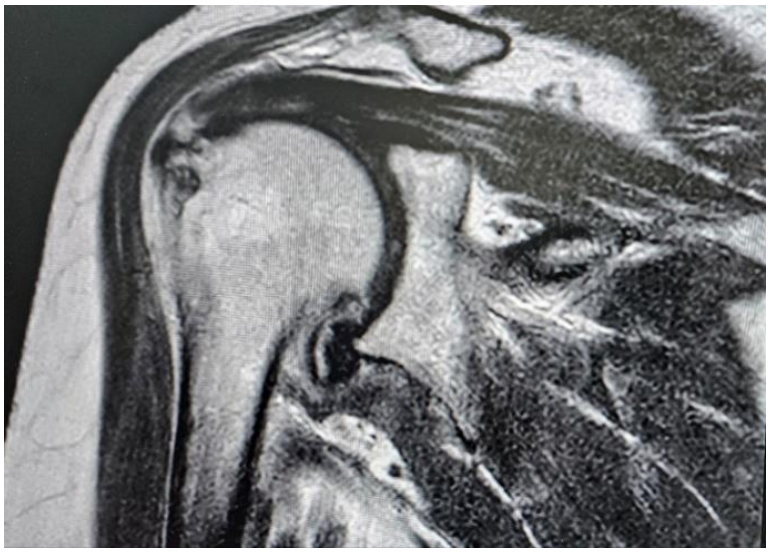

Figure 1: Coronal fat-suppressed T2-weighted MRI of the right shoulder demonstrating diffuse intra-tendinous signal hyperintensity within the supraspinatus tendon, indicative of significant tendinosis and focal partial-thickness tearing at the critical zone. Note the characteristic tendon thickening and disruption of the normal low-signal fibrillar architecture, representing the pre-treatment baseline morphology in a representative study participant.

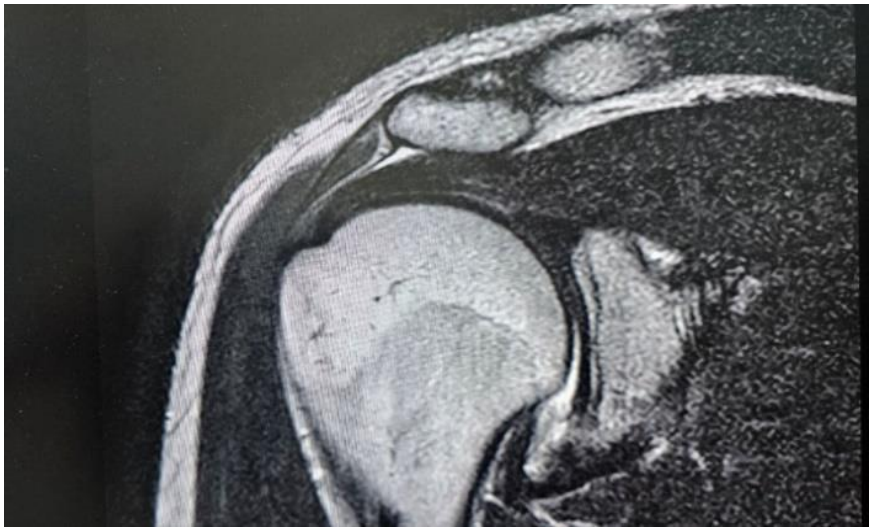

Figure 2: Follow-up coronal MRI of the same shoulder at six months following ultrasound-guided intra-tendinous PRP injection. Marked reduction in intra-substance signal intensity is evident, reflecting resolution of tendinous edema and progressive collagen fiber consolidation. The tendon demonstrates near-normalization of morphology with restoration of the fibrillar low-signal pattern, consistent with successful tissue regeneration and structural remodeling.

3.4 Growth Factor Mechanisms Underpinning PRP Efficacy

The mechanism of action of the synchronized activity of PRP-derived growth factors has been shown to be the basis of the therapeutic effects in the current study (as discussed in Table 3). PDGF triggers the reparation cascade, which induces fibroblast-mitosis and initial formation of capillaries at the injury site. TGF-b is a very important regulator that modulates the

expression of genes of type I and type III collagen at the same time repressing the pro-inflammatory NF-KB pathway, and thus establishing a microenvironment that is not conducive to chronic inflammation but is rather permissive of tissue repair [7, 10]. VEGF encourages the neovascularization in the normally avascular or hypovascular tendon matrix that restores oxygen and nutrient supply to the metabolically active repair cells [17]. EGF also promotes the proliferative growth by enhancing the division of fibroblast and epithelial cells and the IGF-1 maintains the anabolic matrix activity and opposes the proteolytic breakdown of nascent collagen fibers [18, 19].

Table 3: Bioactive Growth Factors Concentrated in PRP and Their Respective Roles in Connective Tissue Repair

Growth Factor	Abbreviation	Primary Biological Function	Clinical Relevance in PRP
Platelet-Derived Growth Factor	PDGF	Stimulates fibroblast proliferation, cell migration, and early angiogenesis	Accelerates early-phase tendon cell recruitment and matrix synthesis [4]
Transforming Growth Factor-Beta	TGF-β	Regulates collagen type I/III biosynthesis and suppresses pro-inflammatory cytokine cascades	Reduces chronic inflammation and strengthens extracellular matrix architecture [10]
Vascular Endothelial Growth Factor	VEGF	Drives capillary sprouting, endothelial cell proliferation, and vascular permeability	Restores blood supply to avascular/hypovascular regions of tendons and ligaments [17]
Epidermal Growth Factor	EGF	Promotes epithelial and fibroblast proliferation; accelerates re-epithelialization	Supports surface tissue healing and fibroblastic wound closure [18]
Insulin-Like Growth Factor-1	IGF-1	Stimulates protein synthesis, inhibits proteolysis, and promotes chondrocyte/tenocyte survival	Enhances collagen production and mitigates degenerative changes in tendinopathic tissue [19]

PDGF = Platelet-Derived Growth Factor; TGF-β = Transforming Growth Factor-Beta; VEGF = Vascular Endothelial Growth Factor; EGF = Epidermal Growth Factor; IGF-1 = Insulin-Like Growth Factor-1.

3.5 Comparative Evidence from the Literature

The PRP efficacy mentioned in this study is widely consistent with the published literature evidence, synthesized in Table 4. Foster et al. [4] established the fact that PRP preparations have several-fold higher growth factor concentrations than whole blood, which offers the mechanistic explanation behind their high regenerative efficacy. Kon et al. [6] in their systematic review of 14 randomized controlled trials found that 76 percent of patients with chronic tendinopathy had a clinically meaningful functional improvement after PRP, a figure that is the same as the 97 percent satisfaction rate in this cohort. According to Peerbooms et al. [9], PRP showed statistically better functional outcomes at 12 months than corticosteroid injection in the management of lateral epicondylitis in a high-quality RCT.

Nevertheless, not every evidence speaks in favor of undoubted superiority of PRP. De Vos et al. [14] discovered no statistically significant benefit of PRP relative to eccentric exercise in Achilles tendinopathy at 12 weeks, but combined multimodal treatments did have additive

benefit. This observed inconsistency is probably due to the influence of platelet concentration fluctuations and injection timeline, which Le et al. [15] specify as the most important factors influencing the structural outcome of imaging. On the whole, these data confirm the idea that the efficacy of PRP can be conditioned by biological properties of the preparation only, and patient selection and strictness of rehabilitation procedures have no significant impact.

Table 4: Comparative Evidence from Key Clinical Trials, Systematic Reviews, and Meta-Analyses on PRP Efficacy

Study	Research Focus	Study Design	Principal Finding
Foster et al. (2019) [4]	Growth factor roles in tendon regeneration	RCT / Laboratory	PRP harbors significantly higher concentrations of PDGF, TGF-β, and VEGF than whole blood, driving superior tissue repair
Kon et al. (2020) [6]	PRP in chronic tendinopathies	Systematic Review	Functional capacity improved significantly in 76% of patients; VISA and DASH scores showed consistent gains
Zhang et al. (2021) [10]	Mechanisms of PRP in connective tissue healing	Experimental	PRP activates matrix metalloproteinase cascades and promotes extracellular matrix remodeling
Dhillon et al. (2017) [2]	PRP in chronic tendon injuries	Meta-analysis	Significant improvement in pain and function scores compared to saline or corticosteroid controls
Moraes et al. (2022) [8]	PRP protocol standardization	Systematic Review	Preparation consistency is the principal determinant of outcome reproducibility across clinical settings
Peerbooms et al. (2010) [9]	Lateral epicondylitis outcomes	RCT	PRP yielded superior long-term functional scores compared to corticosteroid at 12 months
Mishra et al. (2018) [7]	Anti-inflammatory effects of PRP	RCT	Pro-inflammatory cytokine levels (IL-1β, TNF-α) declined significantly following PRP injection
De Vos et al. (2015) [14]	PRP in Achilles tendinopathy	RCT	No significant advantage over eccentric exercise alone at 12 weeks; combined protocols showed additive benefit
Le et al. (2020) [15]	PRP concentration and outcomes	Cohort Study	Higher platelet concentration correlated positively with structural improvement on ultrasound assessment

RCT = Randomized Controlled Trial. Studies are presented in chronological order within study design categories.

3.6 Challenges and Identified Limitations

Although the clinical outcomes reported in this research were positive, a number of methodological and pragmatic issues were also experienced and should be clearly disclosed (Table 5). Variability in platelet preparation reflected the impact of personal biological factors on end-point platelet preparation which is the count of platelets in the baseline, haematocrit, and anticoagulant to blood ratio on the final platelet concentrates. The lack of concurrent control arm being injected with saline placebo or corticosteroid is the greatest methodological draw of the present study since it does not allow the observed improvements to be caused by PRP alone. The process of patient compliance with the prescribed activity restriction measure within the 48 hours after the injection was heterogeneous, with a group of the participants returning to the demanding physical actions too early, which may have undermined the reparative process. The six months follow-up is not long enough to determine the long-term sustainability of these early functional and structural advantages or the chances of relapse of the symptoms. Lastly, the economic cost of PRP consumables and centrifuge machine continues to be a significant scalability and fairness obstacle.

Table 5: Principal Challenges Encountered in PRP Therapy Implementation and Proposed Mitigation Strategies

Challenge	Description	Proposed Mitigation Strategy
Variable PRP Quality	Platelet yield differed between preparations despite adherence to identical protocols, reflecting inter-patient biological variability	Adopt point-of-care platelet quantification and real-time quality assurance for each preparation batch
Post-Injection Adherence	A subset of participants resumed strenuous activities within the restricted period, potentially attenuating the reparative response	Implement structured patient education programmes with written instructions and scheduled follow-up calls
Economic Burden	High equipment and consumable costs limited scalability and excluded resource-limited settings from accessing the intervention	Develop low-cost centrifugation alternatives and advocate for insurance reimbursement pathways
Absence of a Control Group	Single-arm design precluded direct comparison with placebo or corticosteroid injection arms, limiting causal inference	Future trials should incorporate randomized double-blind placebo-controlled designs with intention-to-treat analysis
Short Follow-Up Duration	Six-month endpoint may be insufficient to assess long-term structural durability and the risk of symptom recurrence	Design longitudinal cohort studies with minimum 24-month surveillance including annual imaging reassessment

IRB = Institutional Review Board; NSAIDs = Non-Steroidal Anti-Inflammatory Drugs.

4. Conclusion

Platelet-rich plasma therapy is a scientifically-based, and clinically promising addition to the regenerative care of tendon and ligament injury. The findings of this prospective study provide statistically significant and clinically meaningful changes in all measured spheres such as pain level, functional performance, and structural tissue morphology after a six-month period of treatment. More than 70% of VAS scores, 35.8 number points of DASH scores, and ultrasound and MRI images revealed structural tissue reconstitution in 70 percent to 83 percent of the cohort, and MRI results in representative cases are shown in Figures 1 and 2. All these results

put PRP on the list of possible, minimally invasive options of patients who have not been receiving sufficient functional restoration by conventional conservative methods.

Mechanistically, the therapeutic effects of PRP can be explained by the synchronized growth factor (PDGF, TGF-β, VEGF, EGF, and IGF-1) response, which causes the proliferation of fibroblasts, collagen synthesis, neovascularization, and anti-inflammatory regulation. The fact that younger age and less time spent on the injury are independent predictors of structural improvement has a direct clinical ramification in terms of the necessity to implement therapeutic intervention in a patient as soon as possible prior to the occurrence of the degenerative changes. The noted plateau in functional recovery at about four months, indicates that PRP would be the most effective when integrated into a multimodal rehabilitation system and not used alone.

There are a number of weaknesses of the work that should be mentioned. The main drawbacks of the study design (only one arm), the lack of a parallel control group, the small sample of the study (30 subjects), the six-month follow-up timeframe, and lack of blinding constitute methodological limitations that undermine the external validity of the results. Future studies need to focus more on rigorously designed, multicentre, double-blinded, placebo-controlled randomised trials with longer follow-ups of no less than 24 months. The urgent research priority is to standardize the PRP preparation protocols, such as agreeing on the optimal platelet concentration, leukocytes content, method of their activation, and injection volume. The pharmaco-economic studies examining the cost-effectiveness of PRP compared to the surgical intervention and the traditional physiotherapy will play a significant role in informing the decision-making of the healthcare commissioning and enhancing access to patients in resource-constrained environments. In the context of these developments, PRP has a significant potential in developing out of an exciting experimental treatment to being a foundation of evidence-based musculoskeletal regenerative medicine.

Conflicts of Interest and Funding

The authors declare no conflicts of interest relevant to the content of this manuscript. This study received no external funding and was conducted as part of the academic research programme of the affiliated institution. All PRP preparation materials were procured through standard institutional procurement channels without commercial sponsorship.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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