

Role of Platelet-Rich Plasma (PRP) in Chronic Tendinopathy

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Abstract

Platelet-rich plasma (PRP) is increasingly being used in the treatment of chronic tendinopathy in both sporting and sedentary population. It is rich source of various growth factors and is believed to stimulate and enhance the tissue repair process in tendinopathy. The current literature has six clinical studies (excluding single case studies) which have investigated the effect of PRP in tendinopathy of various tendons. The evidence so far is inconclusive in demonstrating the superiority of PRP over placebo injection or eccentric loading exercises. Future research should focus on conducting randomised controlled studies to establish the clinical effect and support or refute the current widespread use of PRP in chronic tendinopathy.

Key words : Platelet-rich plasma, tendinopathy.

Tendon related disorders account for 30-50% of sport related injuries¹. The term “tendinopathy” refers to a clinical triad of pain, swelling and decreased activity². It was termed tendinitis in the past in the belief that there was an inflammatory component to the condition but it has been shown not to be the case in histological studies. The understanding now is that of collagen disruption with increase in ground substance matrix with abnormal tissue repair and degeneration³.

Among all the available conservative treatment approaches, the best evidence so far is for eccentric loading exercises, which is shown to have positive effect on tendon collagen synthesis and accelerating the reparative process⁴. Platelet-rich plasma (PRP) is a relatively new treatment approach and is now being widely used in the treatment of chronic tendinopathy both in the sporting and sedentary population. The underlying

hypothesis is that platelets derived from whole blood (using a centrifuge system) (Fig 1) is a rich source of various growth factors including platelet-derived growth factor, transforming growth factor- β , vascular-derived endothelial growth factor, epithelial growth factor, hepatocyte growth factor and insulin-like growth factor which can stimulate and hasten the tissue repair process in tendinopathy⁵.

The evidence in this new treatment method has so far been inconclusive. Some recent review articles which included laboratory and clinical studies in tendinopathy

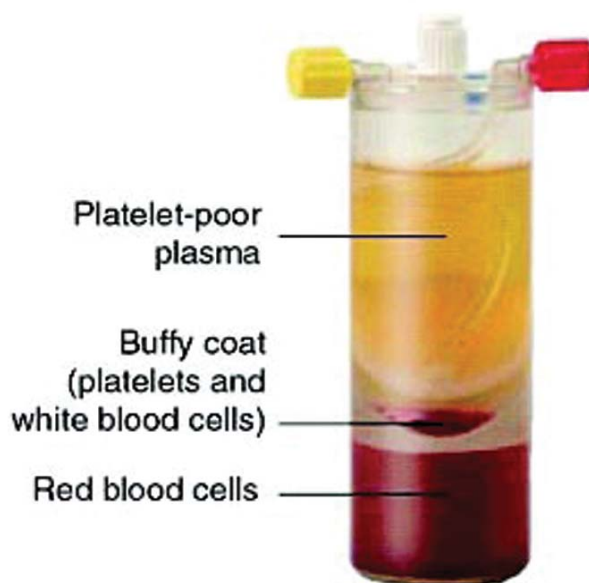


Fig 1 – Post-centrifuge blood sample layers

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concluded significant improvement in pain and functional activity with use of PRP^{6,7}. However, the studies included in these reviews lacked high-quality randomised controlled clinical trials (RCT). Since then, there has been one recent RCT in Achilles tendinopathy with one-year follow-up data which showed no significant effect of PRP over saline injection⁸. The International Olympic Committee (IOC) consensus paper on the use of PRP in sports medicine concludes that there is a lack of convincing evidence to support its use in clinical setting and calls for more research in basic science and robust clinical trials to test efficacy⁹.

This article aims to review the available clinical studies involving the use of PRP to treat tendinopathy. Clinical studies in both sporting and sedentary populations with well-defined outcome measures utilised to measure change have been included in this review. This review will help future research in terms of type of study, participant criteria, sample size, PRP type, imaging and outcome measurement needed to establish the real clinical effect of this treatment.

Summary of Studies:

Six studies were deemed suitable for inclusion in this review. The studies which were not included were single case reports and cases which have investigated the role of augmenting surgical repair of tendon with PRP injection. The methodology of each included study was analysed to derive level of evidence based on recommendations from the Oxford Centre for Evidence-Based Medicine¹⁰. The evidence levels are I: High-quality Randomised Controlled Trial (RCT) or systematic review of level-I RCTs; II: Lesser-quality randomised controlled trial (eg, <80% follow-up, no blinding, or improper randomisation) or Prospective comparative study; III: Case-control study or Retrospective comparative study; IV: Case series; V: Expert opinion. Table 1 summarises the methodology and results of the studies included in this review.

Discussion:

The results suggest the evidence so far is inconclusive for recommending use of PRP in routine practice. The best evidence so far is provided by the RCT by de Vos *et al*⁸ which suggests no enhanced effect over saline injection in Achilles tendinopathy. However, the RCT by Peerbooms *et al* suggests that PRP had a significant enhanced effect when compared to steroid injection in

lateral epicondylitis (tennis elbow). This is supported by another level II study in medial or lateral elbow epicondylitis (golfers or tennis elbow). Finally, two studies from same research group (one level IV study and the other level II study) suggest beneficial effect in patellar tendinopathy.

One could argue that PRP seems to be more effective in non-body weight bearing tendons (common wrist flexor/extensor tendon origin) than body weight bearing tendons (patellar/achilles). In fact, the effect sizes of the intervention have been large with 93% improvement in the study by Mishra *et al*⁶ and 64% in the RCT study by Peerbooms *et al*. The effect size in studies involving patellar tendon or achilles tendon have been smaller. The study in achilles tendinopathy showed no benefit over saline injection⁸ and in patellar tendinopathy, only 54% improvement in EQ-VAS after repeated injections (three in a 6-week period) was observed¹¹.

There is considerable variation in the techniques used in preparation of PRP. There is no standardisation across trials in terms of centrifuge technique, speed and time of centrifuge, apparatus used, storage time and concentration of platelets in the injected PRP. This makes comparability between studies difficult. The IOC consensus statement suggests having a classification system for different PRPs as it might help comparing efficacy among different products⁹. The belief is that the amount and type of growth factors may vary in these different products.

The injection technique varies across the reviewed studies. Most authors used anatomical landmarks to inject PRP in the most tender areas of the tendon. The studies by de Vos *et al*⁸ and Gaweda *et al* however used ultrasound guidance to inject PRP in areas of most hypoechoogenicity within the tendon. de Vos *et al*⁸ though used ultrasound for guiding injection, did not report on the follow-up ultrasound findings. This might have been beneficial to know as this is a level I study and it did not show any difference in outcome between the two groups. Thickness of tendon, echogenicity and neovascularity are key features in ultrasound appearance of tendinopathy and are believed to be related to the severity of the tendinopathy.

All the studies had similar post-procedure rehabilitation programme which included initial rest to gradual buildup of eccentrically loaded exercises. Combining injection with eccentric exercises was utilised in most of the studies. The authors rightly defend that the outcome

Table 1: Summary of Methods, Results and Conclusion of Included Studies

Evidence level	Year	Author	No of patients	Tendon (I) PRP	Intervention group	Control (C)	Outcome measures months	Follow-up	Outcomes (% improvement of PRP)	Conclusion on effect
I	2010	de Vos <i>et al</i>	54	Achilles	1 injection	1 Saline injection	VISA-A (0-100)	6	Mean VISA-A change: 7.8 to 21.7 in I group, 4.6 to 20.5 in C group	Same effect
I	2010	Peerbooms <i>et al</i>	100	Elbow lateral	1 injection	1 Steroid injection	VAS (0-100) DASH	12	Mean VAS change: 65.8 to 50.1 in C group (24%), 70.1 to 25.3 in I group (64%)	Better effect
II	2006	Mishra <i>et al</i>	20	Elbow medial and lateral	1 injection	1 LA injection	VAS (0-100)	25	Mean VAS change: 80.3 to 5.7 (93%) in I group, values not reported for C group	Positive effect
II	2010	Filardo <i>et al</i>	31	Patellar	3 injection	Exercise therapy	EQ-VAS (0-100)	6	Mean EQ-VAS change: 52.7 to 78.3 (54%)	Better effect
IV	2010	Gaweda <i>et al</i>	14	Achilles	1 injection	–	AOFAS VISA-A	18	Mean AOFAS change: 55 to 96, Mean VISA-A change: 24 to 96	Positive effect
IV	2009	Kon <i>et al</i>	20	Patellar	3 injection	–	EQ-VAS (0-100) SF-36	6	Mean EQ-VAS change: 57 to 82 (58%)	Positive effect

cannot be attributed solely to the exercise component of the treatment as the included patients had failed treatment with eccentric exercises prior to the PRP injection. The role of orthosis in the rehabilitation protocol is debatable. The study by Gaweda *et al* had an additional orthosis (heel lift in shoe) to offload the achilles tendon which was not used in the RCT by de Vos *et al*.⁸

Another unknown factor is the ideal time for PRP treatment. It is difficult to conclude from these trials whether this treatment is better suited for treatment of refractory tendinopathy or as an add-on to eccentric exercise rehabilitation programme early in the treatment of the condition. Most of the included studies had patients with failed conservative treatment methods for at least 6 months prior to PRP treatment. It is not known whether including patients at an early stage will lead to improved benefit from the treatment. It might also be interesting to conduct a trial comparing PRP and eccentric exercises,

however the trial cannot be blinded and would be biased by the placebo effect of the injection. Such a trial would have to include a crossover design to overcome such a treatment bias.

There is lack of uniformity in outcome measures used in the studies. The VAS has been used in few studies to capture change in pain intensity. The tendon specific outcomes like VISA-A have been used by de Vos *et al*⁸ and Gaweda *et al*. SF-36 has been used in the study by Kon *et al*, to demonstrate change in general well being. Only one study reports on ultrasound appearances of tendon. In the study by Gaweda *et al*, the changes seen with improvement in pain were reduced thickness of tendon and resolution of hypochoic areas within the tendon. Interestingly the study noted increased neovascularity within and around the tendon with reduction of pain, which is normally not the case with successful treatment of tendinopathy.

Recommendations for Future Research:

In summary, there is lack of substantial evidence to support use of PRP in routine clinical practice. There is need for high-quality RCTs to establish the clinical effect and support the current widespread use.

Two study designs could be considered for future research. First, a double-blind placebo-controlled RCT comparing PRP and saline injection. This will add strength to the findings observed in study by de Vos *et al*⁸. Second, a cross-over randomised controlled trial comparing PRP and eccentric exercises, as there is no study so far which compares PRP to the well proven treatment of eccentric exercises.

The participants should be a homogenous population with similar duration of symptoms and clinical diagnosis. This can include the ultrasound appearance of tendon in terms of presence or absence of discontinuous areas (or defects) in the tendon architecture. The influence of tendon anatomy and biomechanics (upper versus lower limb) on response to PRP needs to be explored.

Using ultrasound to record tendon architectural changes and guiding the injections can help better understanding the tissue response to PRP. No study so far has robust follow-up ultrasound appearance of tendon response to PRP injections.

The preparation and concentration of PRP must be standardised to enable comparability across different studies. Particular emphasis must be placed on platelet concentration, recovery and activation time.

The rehabilitation protocol must be standardised and evidence-based. The type and duration of exercises and equipment used needs to be tendon-specific and uniform for all patients in the study.

Appropriate outcomes to capture pain, functional limitation and return to sport with a long-term follow-up are desirable. A combination of VAS, VISA-A (AOFAS for non-sporting population) and return to sport (SF-36 for non-sporting population) would be ideal to capture change in all domains of the health condition (achilles tendinopathy).

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Abbreviations

VAS	Visual Analogue Scale
VISA-A	Victorian Institute of Sports Assessment-Achilles
DASH	Disabilities of the Arm, Shoulder and Hand
AOFAS	American Orthopedic Foot and Ankle Society
EQ-VAS	EuroQol 5D VAS component
SF-36	Short Form- 36
LA	Local Anaesthetic