

## Platelet-Rich Plasma Injections In The Management Of Chronic Tendinopathies

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**Abstract:** PRP injections have been proposed as a promising alternative for treating tendinopathies. Platelets release various cytokines and growth factors which promote angiogenesis, tissue remodeling, and wound healing. In this study PRP prepared by drawing blood from patient, centrifuging it, prp(3 to 10 times of the whole blood) will be injected over pathological tendon site over maximum point of tenderness, followed by immobilization of the part for 3 days followed by eccentric loading exercise for 6 weeks and results assessed clinically, visual analogue scale at regular interval. PRP injections will be widely accepted by the patient as prepared from patients own blood and risk of adverse effect is minimal. Platelets have known roles in coagulation, inflammatory processes, and immunity modulation. Moreover, during degranulation, platelets release various cytokines and growth factors (vascular endothelial growth factors, platelet derived growth factors, transforming growth factors B, Insulin like growth factor 1 and hepatocyte growth factors) which promote angiogenesis, tissue remodeling, and wound healing. Tendinopathies are chronic affections of the attachments of muscles to the bones.

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### I. Introduction

Tendinopathy refers to a triad of pain, swelling and decreased activity. Tendon related injuries are classified as tendinitis during acute inflammatory process and tendinosis when the healing become chronically impaired, clinicians are increasingly using the term tendinopathy to refer tendon disorders without a specific pathology, and chronic tendinopathy for cases that are refractory to conventional treatment. Common tendinopathies are epicondylitis, rotator cuff tendinopathy, patellar tendinopathy, achilles tendinopathy. These have traditionally been treated conservatively by activity restriction, nonsteroidal anti-inflammatory drugs, physical therapy and judicious use of orthotics. Unresponsive patients are being treated by locally acting steroid injections with varied results. Surgical options are used sparingly when indicated. Platelet rich plasma has been tried by various researchers with the aim of a biological cure with minimal side effects and has shown promising results. Sports related injuries among professional and recreational athletes are increasingly encountered and diagnosed and demand a quick return to preinjury level of sporting activities.<sup>1</sup> "Orthobiologics", refers to the use of biological substances to help musculoskeletal injuries heal quicker. They are used to improve the healing of fractured bones and injured muscles, tendons and ligaments and are derived from substances that are naturally found in body.<sup>2</sup> When they are used in concentrations many times the normal, they can potentially help speed up the healing processes. The substances include bone grafts, autologous blood, platelet-rich plasma (PRP), autologous conditioned serum and stem cells.<sup>2</sup> Bone grafts act by their osteoinductive, osteoconductive and osteogenic properties to stimulate new bone formation and have no effect on the healing of muscles, tendons and ligaments.<sup>3</sup> On the other hand, autologous blood, PRP and autologous conditioned serum deliver growth factors to the diseased areas to stimulate the repair process.<sup>4-6</sup> Platelet-rich plasma (PRP) is defined as a sample of autologous blood with concentrations of platelets above baseline values.<sup>26</sup> Platelets play an instrumental role in the normal healing response via the local secretion of growth factors and recruitment of reparative cells.<sup>59</sup> This study is conducted to know the effect of platelet rich plasma injection in the management of chronic tendinopathy in the Department of orthopaedics, M.K.C.G Medical College, Berhampur from 2014 to 2016.

### II. Aims And Objectives:

To evaluate the efficacy of autologous platelet-rich plasma injection in chronic tendinopathies in terms of relief of symptoms, retention of maximum functional activity, Return to normal work.

#### Inclusion criteria:

All patients presenting with chronic tendinopathies like rotator cuff tendiopathy, epicondylitis, achilles tendinopathy who have failed to improve even after three months of conservative management as outlined above. Men and women between 18 and 75 years of age with tendinopathy for >3 months not resolved with conventional treatment That include epicondylitis, rotator cuff tendinopathy, Achilles tendinopathy

**Exclusion criteria:**

Patients having sensory or neurologic complaints affecting the specified region. Platelet disorder, coagulation disorder, pregnancy, major systemic illness like diabetes, rheumatoid arthritis, fibromyalgia, autoimmune disorders, any condition required strict antiplatelet or anticoagulation therapy., drop out case

**Pre-injection assessment and preparation**

Patients with platelet count less than 1 lakh per millimeters were deferred for 3 weeks and were advised treatment for underlying cause of thrombocytopenia. The deferred patients were not taken for platelet rich plasma preparation till they achieved normal platelet count. Patients having thrombocyte count more than 1 lakh per millimeter were accepted for platelet rich plasma preparation. Patient's blood was taken from ante-cubital vein preferably from left, in tri-sodium citrate vacutainer (3.8%) under sterile precautions directly from vein to vacutainer without opening the vacutainer. Autologous blood was collected in four vacutainer vials (approx. 12 ml) for unilateral tendinopathy. The initial separation of plasma was done by standing method (vial was left in standing position for 1 hour). After 1 hour the vacutainer vials were spun at speed of 1600 round per minute for duration of one minute. Platelet rich plasma (PRP) was seen as the top layer in vial vials followed by yellow buffy coat rich in white blood cells and red blood cell sediment at the bottom. One vial of every patient was used to check quality of platelet rich plasma. Plasma which contained platelet count more than 2.5 times of the patient's blood platelet counts were accepted for injection. This used vial was discarded. One cm plasma of (approx. 0.8-1 ml) which was just above yellow buffy layer was taken from by opening the top cork in a sterile 10 ml syringe and used for injection. Approx 1ml of platelet rich plasma was mixed with 0.5ml lignocaine and used for injection in one tendon. Usually four vial for bilateral and two vials for unilateral cases were adequate. However one to two excess vials preferred were to maintain plasma volume adequacy for injection even in situation error in preparation of plasma, such as hemolysis due mechanical injury to red blood cell during blood withdrawal from patient.

**Platelet rich plasma Injection**

The affected part was cleaned with savlon and painted povidine iodine and draped. Approx. 1.5 ml of mixture of platelet rich plasma and lignocaine was injected in at maximum tender point for epicondylitis and Achilles tendinopathy, and 1 cm below the angle of acromion for RCT. The injection was given with 22 G needle over the part via a peppering technique (single skin entry, partially withdrawing the needle, redirecting and making multiple penetrations to the sheath). After injection the part were immobilized for 3 days with appropriate splints & patients were advised to avoid weight bearing sports activity such as running or jumping and heavy works such as lifting of heavy weights for at least four weeks. Nonsteroidal anti-inflammatory drugs were usually avoided because these drugs may interfere in post injection inflammatory healing process.

**Pre-injection pain assessment**

Visual Analogue Score (VAS) was used to assess pain before injection. All post injection patient were regularly reassessed clinically and for pain improvement with VAS and return to sports activity and heavy work at 1 month, 3 month and 6 month post injection

**III. Analysis**

Data analysis was performed using SPSS version 20. Values are presented as Mean  $\pm$  Standard deviation and standard error of mean. Categorical and Continuous variables were compared using appropriate tests.  $p < 0.05$  is considered statistically significant. Adjusted odds ratio and 95% confidence interval (CIs) will be computed for significant factors.

**IV. Observation**

A total of 50 patients presenting with complaint of chronic tendinopathy, who did not respond to conservative treatment for 3 months, were included in the study. We encounter total eighteen patients of lateral-epicondylitis, nine medial-epicondylitis, twelve rotator cuff tendinopathy and eleven patients of Achilles tendinopathy. Patients with these tendinopathy were advised for autologous platelet rich plasma injection. Advantages and disadvantage (explained in earlier) of platelet rich plasma therapy was explained. 50 of these patients gave valid informed and written consent.

**Table 1 (VAS) for lateral epicondylitis**

Inference: Mean visual analogue score of all lateral epicondylitis at pre injection, at 1 month, 3 month, and 6 month post-injection were 7.55, 6.29, 3 and 1.05 respectively. These values show deceased post injection values.

		Minimum score	Maximum score	Mean	Std. Deviation
VAS	Pre-Injection	6	9	7.55	.7838
	1 Month Post-Injection	3	8	6.29	1.2628
	3 Month Post-Injection	0	6	3	1.878
	6 Month Post-Injection	0	6	1.05	1.696

**Table 2 Descriptive Statistics: Visual analogue pain score (VAS) for medial epicondylitis**

		Minimum score	Maximum score	Mean	Std. Deviation
VAS	Pre-Injection	7	9	7.88	.6009
	1 Month Post-Injection	4	7	5.77	0.9444
	3 Month Post-Injection	0	5	2.88	1.833
	6 Month Post-Injection	0	4	1.444	1.589

INFERENCE: Mean visual analogue score of all medial epicondylitis at pre injection, at 1 month, 3 month, and 6 month post-injection were 7.88, 5.77, 2.88 and 1.44 respectively. These values show deceased post injection values.

**Table 3 Descriptive Statistics: Visual analogue pain score (VAS) for rct**

		Minimum score	Maximum score	Mean	Std. Deviation
VAS	Pre-Injection	8	9	8.25	0.425
	1 Month Post-Injection	5	7	5.75	0.753
	3 Month Post-Injection	2	5	3.58	0.792
	6 Month Post-Injection	0	5	1.25	1.764

INFERENCE: Mean visual analogue score of all rotator cuff tendinopathy at pre injection, at 1 month, 3 month, and 6 month post-injection were 8.25, 5.75, 3.58 and 1.25 respectively. These values show deceased post injection values.

**Table 4 Descriptive Statistics: Visual analogue pain score(VAS) for AT**

		Minimum score	Maximum score	Mean	Std. Deviation
VAS	Pre-Injection	7	9	8	0.447
	1 Month Post-Injection	4	7	5.54	0.82
	3 Month Post-Injection	0	4	3.09	1.136
	6 Month Post-Injection	0	4	1.27	1.555

INFERENCE: Mean visual analogue score of all Achilles tendinopathy at pre injection, at 1 month, 3 month, and 6 month post-injection were 8, 5.54, 3.09 and 1.27 respectively. These values show decreased post injection values.

**Table 5 To check significance difference of mean visual analogues pain score, paired t test were setup between various possible groups as given below for lateral epicondylitis**

MEAN VISUAL ANALOGUES PAIN SCORE		Mean diff.	T value	P value
Pre-Injection	1 Month Post-Injection	1.777	6.20	.00004
Pre-Injection	3month Post-Injection	4.555	11.44	.0000
Pre-Injection	6 Month Post-Injection	6.500	17.044	.0000
1 Month Post-Injection	3month Post-Injection	2.777	5.2	.0000
1 Month Post-Injection	6 Month Post-Injection	4.722	9.7	.0000
3month Post-Injection	6 Month Post-Injection	1.944	4.43	.0001

INFERENCE: There was significant difference of mean visual scores of pain in all given group pair (p value <0.05).

**Table 6 .To check significance difference of mean visual analogues pain score, paired t test were setup between various possible groups as given below for medial epicondylitis**

MEAN VISUAL ANALOGUES PAIN SCORE		Mean diff.	T value	P value
Pre-Injection	1 Month Post-Injection	2.11	6.8	.0001
Pre-Injection	3month Post-Injection	5	10	.0000
Pre-Injection	6 Month Post-Injection	6.44	11.60	.0000
1 Month Post-Injection	3month Post-Injection	2.88	4.27	.0027
1 Month Post-Injection	6 Month Post-Injection	4.33	6.7	.0000
3month Post-Injection	6 Month Post-Injection	1.44	2.87	.0200

Inference: There was significant difference of mean visual scores of pain in all given group pair (p value <0.05).

**Table 7 To check significance difference of mean visual analogues pain score, paired t test were setup between various possible groups as given below for RCT**

MEAN VISUAL ANALOGUES PAIN SCORE		Mean diff.	T value	P value
Pre-Injection	1 Month Post-Injection	2.5	10.8	.0000
Pre-Injection	3month Post-Injection	4.666	20.7	.0000
Pre-Injection	6 Month Post-Injection	7	13.79	.0000
1 Month Post-Injection	3month Post-Injection	2.166	6.73	.0000
1 Month Post-Injection	6 Month Post-Injection	4.5	7.10	.0000
3month Post-Injection	6 Month Post-Injection	2.33	4.84	.0005

INFERENCE: There was significant difference of mean visual scores of pain in all given RCT.

**Table 8 To check significance difference of mean visual analogues pain score, paired t test were setup between various possible groups as given below for AT**

MEAN VISUAL ANALOGUES PAIN SCORE		Mean Diff.	T Value	P Value
Pre-Injection	1 Month Post-Injection	2.45	7.86	.0000
Pre-Injection	3month Post-Injection	4.90	12.52	.0000
Pre-Injection	6 Month Post-Injection	6.72	12.06	.0000
1 Month Post-Injection	3month Post-Injection	2.45	5.4	.0003
1 Month Post-Injection	6 Month Post-Injection	4.27	9.97	.0000
3month Post-Injection	6 Month Post-Injection	1.81	4.54	.0001

INFERENCE: There was significant difference of mean visual scores of pain in all given AT.

**Table 9 Descriptive Statistics: Visual analogue pain score(VAS) for all tendinopathies in our study**

		Minimum score	Maximum score	Mean	Std. Deviation
VAS	Pre-Injection	6	9	7.88	0.6590
	1 Month Post-Injection	3	8	5.72	0.990
	3 Month Post-Injection	0	6	3.14	1.49
	6 Month Post-Injection	0	6	1.22	1.61

INFERENCE: Mean visual analogue score of all tendinopathies at pre injection, at 1 month, 3 month, and 6 month post-injection were 7.88, 5.72, 3.14 and 1.22 respectively. These values show decreased post injection values.

**Table 10**

MEAN VISUAL ANALOGUES PAIN SCORE		Mean diff.	T value	P value
Pre-Injection	1 Month Post-Injection	2.16	14.45	.0000
Pre-Injection	3month Post-Injection	4.74	24.5	.0000
Pre-Injection	6 Month Post-Injection	6.6	28.1	.0000
1 Month Post-Injection	3month Post-Injection	2.58	10.09	.0000
1 Month Post-Injection	6 Month Post-Injection	4.5	16.7	.0000
3month Post-Injection	6 Month Post-Injection	1.92	8.34	.0000

INFERENCE: There was significant difference of mean visual scores of pain in all chronic tendinopathy.

In this study arbitrarily we assumed patient with visual analogue pain score equal or less than 3 as satisfactory improvement of pain.

**Table 11 Percentage of tendinopathie in which satisfactory improvement occurred**

% of patients in which satisfactory improvement of pain			
	1 month post-injection	3 month post-injection	6 month post-injection
Visual analogue pain score	4%	50%	84%

INFERENCE: On basis of Visual analogue pain score, satisfactory improvement of pain at 1 month, 3months and 6month post injection were observed in 4%, 50%and 84% of tendinopathies respectively.

**Summary**

A total of 50 patients presenting with complaints of chronic tendinopathies who did not respond to conservative treatment for 3 months were included in the study. 56% patients were male and 44 % patients were female.in our study 18 (36%), 9 (18%),12(24%) and 11(22 %) of total patients belong to lateral epicondylitis, medial epicondylitis, rotator cuff tendinopathy and Achilles tendinopathy respectively.In this study, 33 (66%) affected patients belong to right side and 17 (34%) affected patients to left side. Mean age of male patient’s was 42.39 ±6.14 year. Mean age of female patient’s was 41.89 ±5.6 year. Most common activity levels in male patients were heavy or longstanding and in female patients were sedentary. There are no significant differences of mean in male and female pain score groups at Pre-injection level.There was no

significant mean difference in preinjection pain scores on basis daily activity level (p value >0.05). Mean visual analogue scores of all affected patients at 1 month, 3 month, and 6 month post-injection follow up showed improvement. Significant difference of mean visual scores of pain were observed.

There was no significant mean difference in male and female patient's pain score. These were no significant mean difference in right and left side pain scores. Satisfactory improvements were shown in 84% of tendinopathies at 6 month follow up on basis of VAS. Satisfactory and unsatisfactory improvement patients had similar profile like age, weight.

## V. Conclusion

The results of this study indicate that PRP injection has a role to play in the management of chronic tendinopathies. This technique was efficient in approximately 84% affected patients at 6 month follow-up. PRP is simple to acquire and prepare and is also cost effective. Hence it provides satisfactory intermediate and long term results in term of pain relief. It seems a safe clinical procedure. Indeed we had no reported side effects. However larger data set and longer follow up are required to conclude definitive role of PRP. We believe that these initial encouraging results now warrant further investigation, in particular with the use of a prospective randomized controlled trial (RCT).

## VI. Limitations

There are some limitations of the study that should be considered. It is small no patients study, only 50 patients. Larger studies would be required to further validate efficacy of autologous platelet rich plasma injection in chronic tendinopathy with failed conservative management. This study did not include any control group for comparison of PRP injection result. Studies with control group of proven treatment modality would be required to further validate efficacy of PRP. In this study PRP preparation was done with ordinary technique. Further Studies with better PRP preparation technique would be required to further validate efficacy of PRP

## VII. Discussion

Chronic tendinopathies are common clinical problem with many available treatment modalities. Traditional treatments include rest, analgesics and physiotherapy. Injections, particularly corticosteroids, are given in very acute situations and for cases unresponsive to conservative methods. Corticosteroids offer a quick fix for pain relief in the acute phase but have limited effect in chronic cases with a significant fraction of patients having relapse and recurrence<sup>130</sup>. In chronic cases, surgery is the last resort with very unpredictable results. Recent years have seen an increase in the use of PRP in various clinical situations like epicondylitis, rotator cuff, patellar and calcaneal tendinopathies, and proximal plantar fasciitis. This study was designed to evaluate the efficacy of PRP therapy for chronic tendinopathy. PRP contains a more concentrated amount of platelets than does whole blood. The rationale for using PRP is to increase tendon regenerative abilities with a high content of cytokines and cells, in hyper-physiologic doses, which should promote cellular chemotaxis, matrix synthesis, and proliferation.<sup>111</sup> Degranulation of the alpha granules in platelets releases many different growth factors that can play a role in tissue regeneration processes. PRP represents a treatment option for many foot and ankle pathologies, including tendinopathy (Achilles, pe-roneal, posterior tibial, flexor hallucis longus, anterior tibial) and chronic ligamentous injury, such as plantar fasciitis.<sup>110</sup> Visual Analogue Scale (VAS) measure amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain. Operationally a VAS is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end.

**Mishra et al (2006)** in their study of prp for lateral epicondylitis taken 15 patients of average age 48.1 yrs showed decreased VAS score(0-100) from 80.3 to 43.4(4 wk) to 32.0(8wk) to 5.7 (6 months). **Hechtman et al (2011)** in their study of prp for lateral epicondylitis showed results of decreased vas score >25 % in 96% of patients at 1 year.

Peerbooms et al.<sup>32</sup> conducted a RCT with 100 patients lateral epicondylitis, 51 of whom received PRP injection and 49 received corticosteroid injections and reported better improvement with PRP over a period of 1 year. Gosens et al.<sup>33</sup> followed up these patients for the subsequent year and reported a sustained improvement with PRP use in comparison to corticosteroids. Thanasas et al.<sup>17</sup> have also shown encouraging results for PRP use compared to ABI in resistant tennis elbow patients. Randelli et al.<sup>36</sup> conducted an uncontrolled pilot study of PRP augmentation along with arthroscopic rotator cuff repair. In their 14 patients injected with PRP activated with thrombin at the tendon footprint after repair, they reported statistically significant improvements in VAS. Owens et al.<sup>47</sup> reported modest improvement in functional outcome in 10 patients who had received PRP injection for mid substance Achilles tendinopathy. Monto et al.<sup>48</sup> reported clinical success in 28 out of 30 patients with recalcitrant Achilles tendinosis. The improvement noted was in the AOFAS score and the MR architecture of the tendon.

The present series also shows significant improvement in VAS in consecutive follow up at 1 month, 3 month, and 6 month of duration for lateral epicondylitis medial epicondylitis and rotator cuff tendinopathy and

Achilles tendinopathy. Differences between mean pain score on follow up were statistically significant in every follow up interval. These results are comparable to previous studies. It was assumed, that patients with visual analogue pain score equal or less than 3. On the basis of Visual analogue pain score, satisfactory improvement of pain were observed in 4%, 50% and 84% of tendons at 1 month, 3 month and 6 month post injection respectively. At final follow up (at 6 month) approx. 84 % of patient who received PRP in injection showed satisfactory improvement of pain.



Figure 1 Requirements

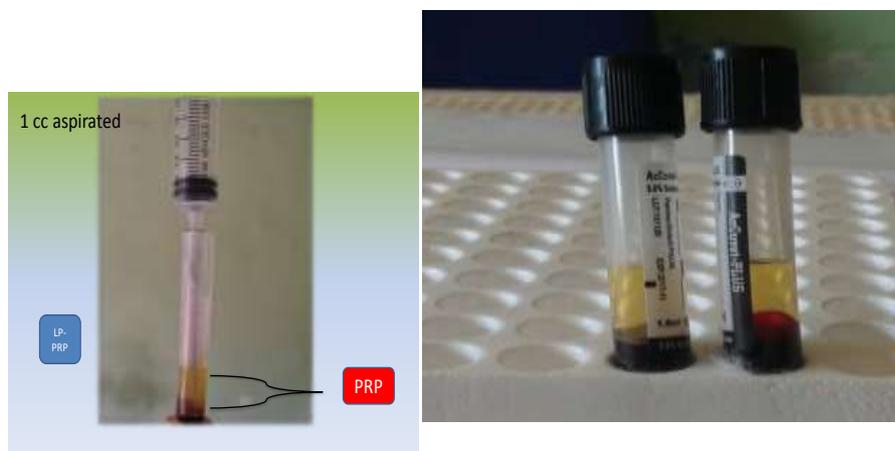


Figure 2 prp separated



Figure 3 mixed with lignocaine



\*PG Student, \*\*Senior Resident, \*\*\* Asst. Professor,\*\*\*Asso Professor, \*\*\*\* Professor

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