

Original Article
Orthopaedics

EFFECT OF PLATELET RICH PLASMA IN MANAGEMENT OF CHRONIC TENDINOPATHIES

Rohit Sharma¹, Rajan Sharma¹, Parampreet Singh², Simarpreet Singh³, Ayush Jain², Lovjot Singh²

¹ - Associate Professor, Department of Orthopaedics, Sri Guru Ram Das Medical College, Amritsar

² - Junior Resident, Department of Orthopaedics, Sri Guru Ram Das Medical College, Amritsar

³ - Senior Resident, Department of Orthopaedics, Sri Guru Ram Das Medical College, Amritsar

Corresponding Author:

Dr. Rohit Sharma
Associate Professor, Department of Orthopaedics,
Sri Guru Ram Das Medical College, Amritsar
Mobile: 09914228888

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Abstract:

Currently, there is no curative treatment for chronic tendinopathies. Non-steroidal anti-inflammatory drugs (NSAIDs) have been the main pharmacological treatment. Autologous platelet rich plasma may present a new therapeutic option for chronic tendinopathies: epicondylitis, rotator cuff, patellar and calcaneal tendinopathies and plantar fasciitis. The study was conducted in Orthopaedics Department of Sri Guru Ram Das Medical college and Hospital, Amritsar on patients in the outdoor department here for treatment of chronic tendinopathies to evaluate clinical effects of single injection of platelet rich plasma (PRP) in symptomatic patient with chronic tendinopathy using VAS score, with a follow up period of upto 1 year. We concluded that autologous PRP injection is an acceptable method to relieve pain. Due to the autologous nature of PRP there are very less chances of complication, thus we recommend PRP injection as a simple, minimally invasive, safe and an effective alternate method which can be used for the management of chronic tendinopathies.

Key words: Platelet Rich Plasma, Management Chronic Tendinopathies

Introduction

Tendons are the load-bearing attachments of muscles into bones that allow a muscle contraction to translate into mechanical movement of the skeleton. They originate at the myotendinous junction, where the tendon fibers are intertwined into deep recess between the muscle fibers, and insert into the enthesis, defined as the fibrocartilage interface between the tendon fibers and the bone.

Tendons are the strongest soft tissue structures in the human body in terms of resisting tensile strength, capable of supporting up to 12 times the body's weight.¹ This strength comes from the tendon's structure, which is mostly made up of collagen fibers alligned parallel to each other. The maximum tensile strength that a tendon can withstand is directly proportional to the number of collagen fibers and the thickness of the tendon. The ongoing tensile stress that tendons experience on a daily basis stimulates the tenocytes, which are the main cells found in tendons, to maintain the optimal ratio of collagen fibers to noncollagenous structures in the tendon.

Lower extremity tendon injuries frequently progress to chronic tendinopathies. Multiple extrinsic and intrinsic factors may contribute to suboptimal healing, pain, and dysfunction. Platelet rich plasma (PRP) injections have been shown to restore the healing process and provide significant improvement in both pain and functional scores. PRP is considered an ideal autologous blood product that promotes the body's own natural healing.² This concentrate has been used for more than 25 years in oral and maxillofacial surgery, otorhinolaryngology, plastic surgery, and general surgery,

with multiple case series reports showing overall improvement in soft tissue healing.³⁻⁴ It has recently become popular for management of musculoskeletal injuries based on in vitro studies reporting an enhancement of the recruitment, proliferation, and differentiation of the cells involved in muscular tissue regeneration.⁵ Furthermore, randomized controlled trials, prospective case series, and case control studies detailed below have shown successful clinical outcomes in treating different types of lower extremity tendinopathies.

Autologous PRP Injection

Research is studying innovative approaches of stimulating repair or replacing damaged cartilage and studies regarding tissue biology have highlighted a complex regulation of growth factors (GFs) for the normal tissue structure and the reaction to tissue lesions.⁶ In fact, the role of GFs in chondral repair is now widely investigated in vitro and in vivo.^{7,8}

Platelet-rich plasma (PRP) therapy involves injecting a solution of the patient's own concentrated blood components (especially platelets) into their tendons: the aim is to promote cartilage repair and relieve symptoms. Platelet Rich Plasma (PRP) injection, a novel approach, gives significant improvement in tendinopathy due to the presence of autogenous growth factors and attract the Mesenchymal stem cells so as to start the chondroprotective and chondroregenerative potential in and around the joint. Mesenchymal stem cells (MSCs) are the focus for the development of many cell-based therapies for a diverse array of diseases, and are a subset of nonhematopoietic adult stem cells that originate from the mesoderm and

exist in almost all adult tissues.⁹ MSCs have been demonstrated to secrete a broad range of bioactive or trophic factors that are essential in the cellular microenvironment for survival, protection, immune modulation, and differentiation effects.¹⁰ Platelet alpha-granules contain over 30 growth factors.

Table 1 - Summary of the effect of growth factors on chondrocytes/cartilage, synovioma, and mesenchymal stem cells in vitro and in vivo¹¹

Growth factor	Chondrocytes/cartilage	Synovium	Mesenchymal stem cell
TGF-b1	Stimulates synthesis of ECM Decreases catabolic activity of IL-1 and MMPs	Causes synovial proliferation and Fibrosis Induces chemotaxis of inflammatory leukocytes to synovium Induction of osteophyte formation	Increases proliferation and ECM production Down regulates collagen type 1 gene expression
BMP-2	Stimulates synthesis of ECM Partial reversal of dedifferentiated phenotype in OA Increased ECM turnover (increased aggrecan degradation)	Presumed role in maturation of osteophytes Multiple injections lead to synovial fibrosis Stimulates synovial thickening in experimental OA	Increases proliferation and ECM production Down regulates collagen type 1 gene expression
BMP-7	Stimulates ECM synthesis Decreases cartilage degradation through decreasing activity/ expression of numerous ILs and MMPs	Decreases expression of MMPs and aggrecanase Does not appear to cause osteophyte formation or synovial fibrosis	Inhibits cell proliferation Inconsistent ability to induce chondrogenesis Alone Potentiates chondrogenic differentiation with TGF-bs resulting in increased ECM synthesis and decreasing collagen type 1 compared with TGF-b alone
IGF-I	Stimulates ECM synthesis Decreases matrix catabolism except in aged and OA cartilage	Protective effect on synovium resulting in decreased thickening and decreased evidence of chronic inflammation	Stimulates cell proliferation Increases expression of ECM Additive effect when combined with TGF-b
FGF-2	Decreases aggrecanase activity Antagonizes PG synthesis Up regulates MMPs	Induces synovial proliferation Inflammatory and induces osteophyte formation when used alone	Increases PG synthesis Increases cell proliferation
FGF-18	Increases chondrocyte proliferation and stimulates ECM in vitro and in injured joints but not in normal joints	Induces synovial thickening Enlargement of chondrocytes in experimental OA	
PDGF	No adverse effect in normal joints	No adverse effect in normal joints	Induces proliferation

TGF-b1 = transforming growth factor-b1; BMP = bone morphogenetic protein; IGF-I = insulin growth factor I; FGF = fibroblast growth factor; PDGF = platelet-derived growth factor; ECM = extracellular matrix; IL = interleukin; MMP = matrix metalloproteinase; OA = osteoarthritis; PG = proteoglycan.

PRP can be defined as the volume of the plasma fraction from autologous blood with platelet concentration above baseline count (200,000 platelets per/micro Litre).¹² The rationale for the use of PRP is to stimulate the natural healing cascade and tissue regeneration by a

“supraphysiologic” release of platelet-derived factors directly at the site of treatment. The term “activation” refers to two key processes within GFRP preparations that may be initiated: (1) degranulation of platelets to release granules containing growth factors and (2) fibrinogen cleavage to initiate

matrix formation.

Accordingly, platelet activation can be achieved by the following 3 mechanisms:

1. Addition of calcium chloride and thrombin
2. Freeze/thaw cycles,
3. Direct exposure to collagen in

vivo. Non activated GFRP can be injected directly into the injured tissue, which becomes activated on contact with collagen. Collagen is one of the most potent activators of platelet adhesion and aggregation. In vivo collagen activation is the preferred method for activating GFRP, as it leads to a slower and more sustained release of growth factors, compared with the thrombin method.

PRP is a simple, low cost and minimally invasive method to obtain a high concentrate of autologous GFs in physiological proportions, which can be easily and safely placed directly into the lesion site. Moreover, the risk of allergy or infection is negligible, due to the autologous nature of the platelet extract.¹⁴ Platelet-rich plasma (PRP) is one therapeutic application with promising preliminary clinical results.^{14,15,16}

Material And Methods

The study was conducted in Orthopaedics Department of Sri Guru Ram Das Medical college and Hospital, Amritsar on patients in the outdoor department here for treatment of chronic tendinopathies. 30 patients of either sex were selected for this study in the age group of 30-60 years. The informed consent of each patient was taken on the prescribed proforma. This study was undertaken after due approval by the Ethics Committee.

The 30 selected patients of chronic tendinopathies were examined as per proforma attached. Pain was assessed as per the clinical finding.. All the patients were treated with 1 intra-articular injection of Autologous PRP. Patients were discharged immediately after the procedure. Following discharge from the hospital, the participants were followed up on a regular basis with

clinical examinations and functional evaluations for pain relief as per VAS scale . All examinations were taken at 3 month, 6 months and 12 months. The standard blood investigations before treatment would be Complete Blood Count (CBC), Coagulation profile(BT,CT) and test for transfusion transmissible diseases (TTI).

Inclusion Criteria:

1. Age between 30 and 60 years, body mass index <30, normal results for complete blood count and coagulation control, minimum follow-up of 6 months.
2. Patients with chronic tendinopathy based on clinical findings.
3. Patients with severe pain and under anti-inflammatory treatment without improvement > 3 months.
4. Patients who gave consent for treatment with platelet-rich plasma per our protocol.

Exclusion Criteria

1. Patients with platelet dysfunction syndrome, critical thrombocytopenia, immunodeficiency, hepatitis B or C, HIV-positive status, septicemia and local infection.
2. Clinical signs of acute inflammation(possible infection or infection)
3. Pretreatment platelet count <150/ul and HGB <10g/dl.
4. Intake of alcohol in the last 24 hours.
5. Consistent use of NSAIDs within 48 hours of procedure, Corticosteroid injection at treatment site within 1 month or Systemic use of corticosteroids within 2 weeks.
6. History of intake of antibiotics within 48 hours of procedure.

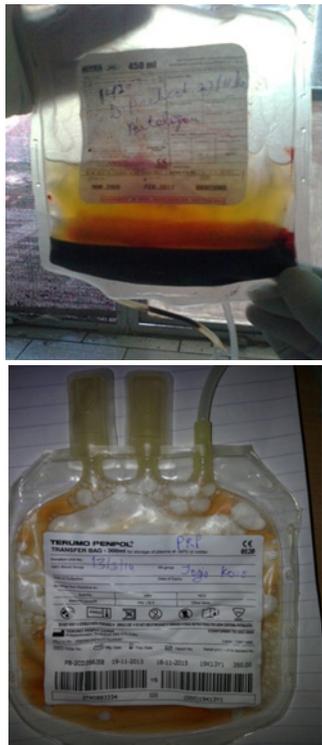
Preparation of PRP

On the day of the procedure, the

patient was taken to the Blood Bank, SGRDIMSR, Amritsar. A double bag was taken, and 48 ml of CPD (citrate phosphate dextrose) was removed and discarded, leaving just 15 ml of CPD-A1 in the bag. 100mL of venous blood was drawn into the 1st chamber of adult double bag with 14ml CPD-A1 (citrate phosphate dextrose and adenine) as an anticoagulant under aseptic precautions from the antecubital vein a traumatically. This bag then underwent two centrifugations (the first at 1,800 rpm for 15 min to separate erythrocytes at the bottom and the plasma above, and a second at 3,500 rpm for 10 min to concentrate platelets) to produce about 15 ml of PRP. The final PRP will be taken for injection in a 10-mL syringe and sample were sent to lab for assessment of platelet count.



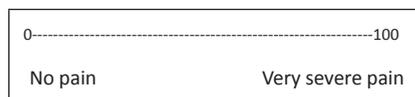
Presvac Cryofuge



Interventional Procedure:

All patients were treated with 1 injection of PRP at the site of maximum tenderness. Under aseptic conditions, 8 mL of plasma concentrate were injected with an 18-gauge needle. At the end of procedure, the patients were encouraged to stretch the tendon a few times, to allow the PRP to distribute itself throughout the joint before becoming gel. After the injection, the patients were sent home with instructions on limiting the use of the limb and not to use nonsteroidal medication but to use cold therapy for pain for at least 24 hours. After discharge from the hospital, the patients were followed up at 3, 6 and 12 months and clinical outcome was evaluated using Visual Analog Scale (VAS).

VAS



Before the injection the pain was

considered at 100 mm in all patients and at every follow up; patient was asked to mark a point on the line to explain how much of pain relief he/she is having.

Results evaluation as per VAS Scale improvement

Excellent	> 80%	Improvement
Good	60- 80%	Improvement
Fair	40- 60%	Improvement
Poor	< 40%	Improvement

Before the injection and at every follow up; patients were asked questions regarding pain, stiffness and physical function to calculate the total score.

The comparative evaluation of the results of clinical outcome of Autologous PRP injection at every follow from baseline was done.

Quantitative variables were described using mean standard deviation (SD) and categorical data by percentage. In all tests, p value <0.05 was considered to be statistically significant. Following results were observed at different follow ups.

Results

The youngest patient in the study was 35 years old and the oldest was 60 years old. Average age was 49.7 years. Majority of the patients (47%) were in the age group of >50 years and four patients were in the age group of <40 years.

Age Distribution

Age group (years)	No. of cases	% age
<40	4	13.33
41-50	12	40.00
>50	14	46.67
Total	30	100.0
Mean Age	49.76±6.60	

Females outnumbered males in presenting complaints. 18 (60%) patients were females and 12 (40%)

were males. Female to male ratio was 6:4.

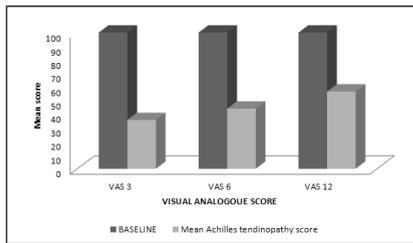
VAS Scores

VAS score was considered as 100 in all the patients at the start .After injecting the single PRP injection, patients were asked to mark a point for the level of pain on a straight unmarked line 100 mm long at a later follow up period of 3 months, 6 months and at one year interval after the PRP injection being given.Once the marking was done by the patient,it was measured with a measuring scale to know the VAS score. Lesser the VAS score better was the pain relief. The VAS scores for various tendinopathies were calculated and their difference were compared to yield a statistically computing score (p value),which was then quanted upon as significant(P<.05) or insignificant.

Achilles Tendinopathy

At 3 months, VAS remained at 40 mm and mean score of 35.8 and standard deviation of 4.9 was observed. At 6 months VAS remained at constant 45 mm and mean score of 44.1 and standard deviation of 7.8. At one year interval VAS remained constant at 65 mm and mean score of 56.6 and standard deviation of 0.08 was seen.

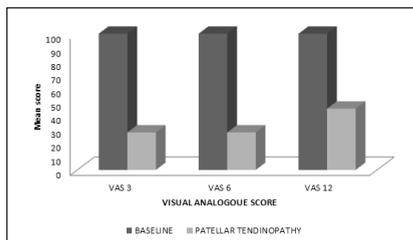
The difference in VAS score at 3 and 6 months follow up came out to be statistically significant with p value=0.004(p<0.05). The difference in the VAS score at 6 months and one year follow up remained statistically significant with p value=0.006.At the final follow up the Vas score at 3 months and one year interval were statistically significant with p value=0.001.



Patellar Tendinopathy

At 3 months, VAS remained at 40 mm and mean score of 27.5 and standard deviation of 3.5 was observed. At 6 months VAS remained at constant 45 mm and mean score of 27.5 and standard deviation of 3.5. At one year interval VAS remained at 65 mm and mean score of 45.0 and standard deviation of 0.0 was seen.

We found statistically insignificant difference in VAS score at 3 and 6 months follow up with p value=1.0(p<0.005). However there was significant difference in the VAS score at 6 months and one year follow up with p value=0.02. At the final follow up the Vas score at 3 months and one year was found to be statistically significant with p value=0.02

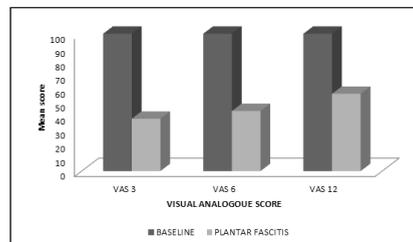


Plantar Fasciitis

At 3 months,VAS ranged between 25 mm and 50 mm and mean score of 38.12 and standard deviation of 9.23 was observed. At 6 months VAS ranged between 15 mm and 35 mm and mean score of 43.75 and standard deviation of 11.57. At one year interval VAS ranged between 40 mm and 50 mm and mean score of 56.25 and standard deviation of 10.93.

In our study statistically insignificant difference was seen in

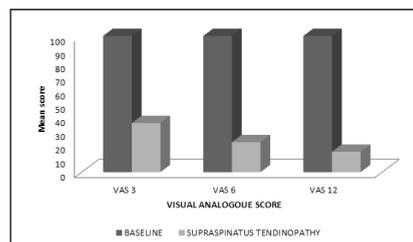
VAS scores at 3 and 6 months follow up with p value=0.301. Statistically significant difference was seen in the VAS scores at 6 months and one year follow up with p value=0.043. At the final follow up on comparing the Vas scores at 3 months and one year interval statistically significant difference was seen with p value=0.003.



Supraspinatus Tendinopathy

At 3 months,VAS ranged between 25 mm to 55 mm and mean score of 36.0 and standard deviation of 13.4 was observed. At 6 months VAS ranged between 15 mm and 30 mm and mean score of 22.0 and standard deviation of 6.7 was seen. At one year interval VAS ranged between 10 mm to 20 mm and mean score of 15.0 and standard deviation of 3.5 was seen.

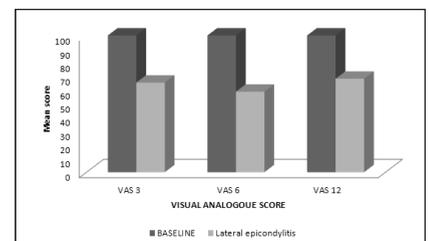
Our study showed statistically insignificant difference in VAS score at 3 and 6 months follow up with p value=0.070. Also there was no significant difference in the VAS score at 6 months and one year follow up with p value=0.073. However at the final follow up the difference in Vas scores compared at 3 months and one year interval were found to be statistically significant with p value=0.001.



Lateral Epicondylitis

At 3 months,VAS ranged between 55 mm to 85 mm and mean score of 65.55 and standard deviation of 16.47 was observed. At 6 months VAS ranged between 45 mm and 80 mm and mean score of 58.88 and standard deviation of 12.69 was seen. At one year interval, VAS ranged between 55 mm and 75 mm and mean score of 68.33 and standard deviation of 6.12 was seen.

Results in our study showed statistically insignificant difference in the VAS scores at 3 and 6 months follow up with p value=0.351. Also there was no significant difference in the VAS scores at 6 months and one year follow up with p value=0.062. At the final follow up on comparing the Vas scores at 3 months and one year interval statistically insignificant difference was found with p value=0.344



Summary And Conclusion

The present study was conducted to determine the effect of platelet rich plasma (PRP) in treatment of chronic tendinopathies. The results obtained were evaluated according to standard statistical analysis and the following conclusions were made:

1. Majority of the patients were between the age group of 50-60 years. Only four patients were in the age group of <40 years. The average recorded age was 49.7 years.
2. Females outnumbered males in presenting with pain due to

chronic tendinopathies. Female to male ratio was 6:4.

3. 50% of the cases had right side involvement and left side involvement also comprised 50% in all cases.
4. Achilles tendinopathy showed statistically significant difference in VAS ($p < 0.05$) at 3 months, 6 months and at one year interval showing good results of PRP injection in their management.
5. Lateral epicondylitis showed in significant difference in VAS at 3 months, 6 months and at one year interval giving poor results in effectiveness of PRP in Lateral epicondylitis.
6. Patellar Tendinopathy VAS were significant statistically at 6 months and at one year interval showing PRP as efficacious in treating it.
7. Plantar fasciitis showed insignificant statistical difference in VAS at 3 months and 6 months ,however the difference in VAS at 3 months and one year interval were statistically significant .
8. Supraspinatus tendinopathy showed significant statistical difference in VAS at 3 months and one year interval ($p < 0.05$)
9. No major complication of any form was noted in any of the patient except post procedure pain for about 24 hours in 60% of patients and one patient experienced stiffness at the elbow joint after the procedure.
10. No superficial or deep infection was noted in any of the patients.

It is inferred from the above observations that majority of the patients of chronic tendinopathies seek medical intervention for their

pain relief in the 5th decade of their life and when the problem is slightly prolonged.

PRP injection takes some time to induce the action and hence the onset of pain relief is slow but long lasting which is clearly shown in the results at different follow up in all patients.

We concluded that autologous PRP injection is an acceptable method to relieve pain.

Due to the autologous nature of PRP there are very less chances of complication, thus we recommend PRP injection as a simple, minimally invasive, safe and an effective alternate method which can be used for the management of chronic tendinopathies.

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