Original Article

Journal of Orthopedic Education
Volume 7 Number 1, January – June 2021
DOI: http:// dx.doi.org/10.21088/joe.2454.7956.7121.2

Platelet Rich Plasma or Steroid for tendinopathies: A Randomised Control Trial

[1]Imran H Khan, [2]Vinod Singh, [3]Vikram Nigam

How to cite this article:
Imran H Khan, Vinod Singh, Vikram Nigam, Platelet Rich Plasma or Steroid for tendinopathies: A Randomised Control Trial. J orth. Edu. 2021;7(1):17–21.

Author's Affiliations: [1]Junior Resident, [2]Senior Resident, [3]Associate Professor, Department of Orthopedics, Moti Lal Nehru Medical College, Prayagraj, Uttar Pradesh 211002, India, India.

Corresponding Author: Vikram Nigam, Associate Professor, Department of Orthopedics, Moti Lal Nehru Medical College, Prayagraj, Uttar Pradesh 211002, India, India.

Email: imran786a@gmail.com

Abstract

Context: Tendinopathy, mostly seen in athletes, is becoming common in sedentary population also. Orthopaedics now focuses on biological repair, like Platelet Rich Plasma (PRP), to keep native structure intact. ***Aims:*** Compare efficacy of PRP and steroid in treating tendinopathies. ***Settings and Design:*** Parallel group randomized control trial was conducted in Orthopaedics Department tertiary care hospital in North India over one year. ***Methods and Material:*** Clinical and radiological diagnosis of tendinopathy was made. Patients received PRP or steroid according to their group allocated. Functional status and severity of pain around injured joint was charted pre-procedurally on day 0 and post procedurally at end of 6 weeks, 12weeks, 24 weeks and 48 weeks based on clinical and radiological examination. ***Statistical analysis used:*** Mean and standard deviation of scores for both modalities of treatment was compared. ***Results:*** Forty patients were analysed in PRP group and 52 patients were analysed in steroid group. Both VAS and FFI score decreased in both type of injuries in both the modalities of treatment from pre procedure evaluation till 48weeks after therapy. In plantar fasciitis, the improvement seen in PRP group was more marked than that seen in steroid group ($p<0.05$). Similarly, for retrocal caneal bursitis with Achilles' tendinopathy, the improvement in DASH and VAS score was statistically significant in the PRP group. ***Conclusions:*** Patients who received PRP showed better clinical results (reduction in pain, swelling and improved range of motion) as compared to patients who received steroid. Former also had higher satisfaction level because of improved functional status as well as relief of local symptoms which led to improved quality of life.

Keywords: Platelet Rich Plasma; Steroid; Tendinopathy.

Key Messages: Use of platelet rich plasma provides better and safer alternative to steroid for the treatment of tendinopathies.

Introduction

Tendinopathies present as pain in injured tendon, aggravating with palpation or active and passive movements involving the concerned tendon. They make up for about 30% of healthcare consultations1. Tendinopathy is most often seen in tendons of athletes either before or after an injury but is becoming common in non-athletes and sedentary population. Various type of treatments has been recommended like rest, activity modification, NSAIDs, steroid, braces, massage etc. However, focus in orthopaedic surgery is changing rapidly with idea of biological repair of injured tissue to keep the native structure intact. One such treatment modality is use of Platelet rich plasma (PRP). PRP is autologous blood product derived from whole blood of the patient. PRP when injected into an area of inflammation/degeneration brings about healing of the injury.

Platelets release many bioactive proteins and growth factors resulting in recruitment of macrophages, mesenchymal stem cells and osteoblasts which promote necrotic tissue removal, improve tissue regeneration and healing. PRP induces proliferation of two tendon cell types, tenocytes (which help in tendon repair) and tendon stem/progenitor cells (TSCs), by induction of vascular endothelial growth factor and hepatocyte growth factor (HGF).[2,3,4] PRP also accelerates proliferation of bone marrow stem cells and adipose

Healing.[2,5,6] HGF reduces levels of pro inflammatory mediators like COX-1, COX-2, IL-6, IL-8 and PGE2[7,8] and increases anti-inflammatory cytokines like IL-10 and TGF-β which restricts local inflammation.[9] PRP by its anabolic effects, increases collagen production thereby helping extracellular matrix restoration and tissue remodelling in healing tendons. Plasma in PRP positively influences cell attachment and its spread on fibrin scaffold.[10]

This study aims to compare functional outcome of treatment with PRP against steroid therapy; hence establish the role of PRP in management of tendinopathies and bursitis.

Materials and Methods:

This parallel group randomized control trial with 1:1 case allocation in two groups was conducted in department of Orthopaedics of a tertiary care hospital in North India over one year. Approval from institutional ethical committee was obtained to carry out the study. With 30% prevalence of tendinopathies among total Orthopaedic outdoor patients, 80% power of study and alpha=0.05, sample size was calculated as 90 cases. Patients were selected from Orthopaedic outdoor and indoor ward. Patients with retrocalcaneal bursitis, Achilles tendinopathy, lateral epicondylitis and planter fasciitis were included in the study. Patients with any evidence of tear in concerned tendon, arthritis of nearby joint, pre-existing local infection, peripheral vascular disease, rheumatoid arthritis, spondylo-arthropathy were excluded from the study. Those suffering from bleeding or coagulation disorder, uncontrolled diabetes mellitus, hypertension and patients not giving consent to participate were also excluded. Informed and written consent was obtained from enrolled patients after explaining them about the study in their local language. All eligible subjects were randomly assigned to receive either PRP (Group 1) or steroid (Group 2). Block randomization was done using computer software (http://www.randomizer.org/form.html). Allocation was done through sequentially numbered opaque sealed envelopes (SNOSE technique). Only blinding of data analyser was possible due to the method of study.

On enrolment, history was elicited from patients. They were assessed clinically to evaluate their general condition, vitals and clinical signs. Base line investigations (hemoglobin, total and differential leukocyte count, blood sugar, bleeding and clotting time, serum electrolytes, renal function tests, HIV, HBsAg and anti HCV) were done. X-ray of concerned site was done to rule out osseous pathology. Ultrasonography and MRI was done, if required. A clinical and radiological diagnosis of tendinopathy was made. The patients received PRP or steroid according to their group allocated.

For PRP, ten ml venous whole blood of the patient was obtained by venepuncture in acid citrate dextrose tube. Blood was not chilled at any time before or during platelet separation. Blood was first centrifuged using a 'soft' spin (ten minutes at 3000 RPM) to separate packed cells from plasma. The supernatant plasma containing platelets was transferred into another sterile tube (without anticoagulant). It was centrifuged at a 'hard' spin (5000 RPM for ten minutes). The lower 1/3rd obtained is PRP and upper 2/3rd is platelet-poor plasma (PPP). At the bottom of tube, platelet pellets are formed. PPP was removed and platelet pellets was suspended in minimum quantity of plasma (2-4 mL) by gently shaking the tube. Active PRP was prepared just before use. Every 20cc of venous blood yielded 3-4 ml of PRP11. Ideal concentration is at least four fold increase in initial concentration (around one lakh mm). All cases in Group 1 were injected 3-4 ml of autologous PRP maintaining all aseptic precautions.

In group 2, one ml injection Trimacinolone acetonide (40mg\ml) is mixed with two ml of 1% lignocaine (to reduce immediate post injection pain) and diluted in three ml normal saline. It is injected along inflamed tendon at area of maximum tenderness.

Routine antibiotics and analgesics were administered after PRP/steroid injection. Sterile dressing was applied at injection site. Patients were trained for home based joint exercises. They were advised for protected weight bearing for minimum two weeks and pain was combated with ice pack application.

Functional status and severity of pain around the injured joint was charted pre-procedurally on day 0 and post procedurally at end of 6 weeks, 12weeks, 24 weeks and 48 weeks based on clinical and radiological examination. VAS (Visual Analogue Scale), DASH (Disabilities of the Arm, Shoulder and Hand) score and FFI (Foot Function Index) score were used to assess the efficacy of therapy. Mean and standard deviation of the scores for both the modalities of treatment was compared and p value <0.05 was taken to be statistically significant.

Results:

Figure 1 shows the patient recruitment. Over the study period, 211 patients with trauma were screened for inclusion in study. Out of these, 109 patients were excluded due to various reasons (Figure 1).

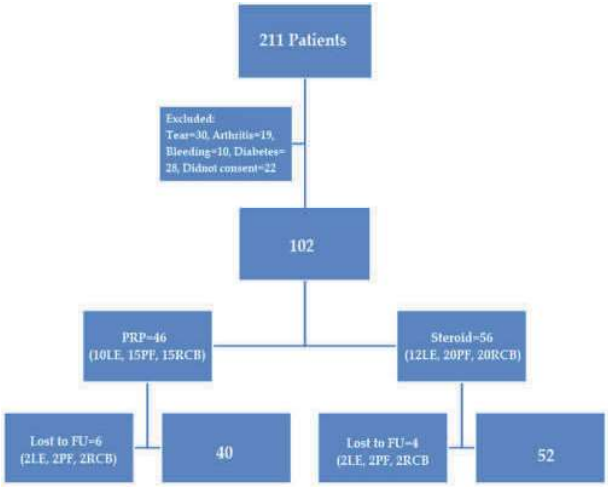

Figure 1: Patient recruitment flowchart.

Table 1: Baseline characteristics of patient.

Disease	Total patients	M	F	Mean age (years)
Lateral epicondylitis	PRP=10 Steroid=12	PRP=6 Steroid=9	PRP=4 Steroid=3	PRP=35.5 Steroid=30
Plantar fasciitis	PRP=15 Steroid=20	PRP=5 Steroid=11	PRP=10 Steroid=9	PRP=31.4 Steroid=33.6
Retrocalcaneal bursitis with Achilles' tendinopathy	PRP=15 Steroid=20	PRP=8 Steroid=10	PRP=7 Steroid=10	PRP=33.6 Steroid=36.25

The remaining 102 patients were randomly assigned to the two groups. Six patients were lost to follow up in PRP group and four were lost in steroid group. Finally, 40 patients were analysed in PRP group and 52 patients were analysed in steroid group. The baseline characters of both the groups are listed in Table 1.

As shown in Table-2, among 22 patients of lateral epicondylitis randomized for the study, ten received PRP and 12 received steroid therapy. Both VAS and DASH score were decreased in both the groups from pre procedure evaluation till 48weeks after therapy. But the improvement seen in PRP group was more marked than that seen in steroid group. There was significant difference in the VAS and DASH score between the two groups at the end of 48weeks post therapy ($p<0.01$).

Table 2: Scores for Upper limb tendinopathies.

Lateral epicondylitis	Method	Pre-procedure (Mean ±SD)	6 weeks (Mean ±SD)	12 weeks (Mean ±SD)	24 weeks (Mean ±SD)	48 weeks (Mean ±SD)
VAS score	PRP	7.10±0.83	4.81±0.78	4.60±0.70	3.21±0.78	2.31±0.67
	Steroid	7.08±0.79	5.12±0.83	5.83±0.94	5.61±0.88	4.91±0.79
DASH score	PRP	54.52±1.73	43.0±1.38	29.07±1.69	14.26±1.59	8.30±1.12
	Steroid	57.36±1.73	44.95±1.62	34.53±3.44	22.02±5.27	15.89±8.22

SD: standard deviation

Table 3 shows that among 90 patients of lower limb injury randomized for the study, 45 had plantar fasciitis and 45 had retrocalcaneal bursitis with Achilles' tendinopathy. Fifteen patients in both the types of injury received PRP and ten in both received steroid therapy. Both VAS and FFI score decreased in both type of injuries in both the modalities of treatment from pre procedure evaluation till 48 weeks after therapy. In plantar fasciitis, the improvement seen in PRP group was more marked than that seen in steroid group ($p<0.05$). Similarly, for retrocalcaneal bursitis with Achilles' tendinopathy, the improvement in DASH and VAS score was statistically significant in the PRP group as compared to steroid group ($p<0.05$).

Table 3: Scores for Lower limb tendinopathies.

Disease	Method	Pre-procedure (Mean ±SD)	6 weeks (Mean ±SD)	12 weeks (Mean ±SD)	24 weeks (Mean ±SD)	48 weeks (Mean ±SD)
			VAS score			
Plantar fasciitis	PRP	6.86±0.83	4.86±+0.83	4.06±1.03	3.33±0.72	2.33±0.62
	Steroid	7.15±0.74	5.80±0.81	5.42±0.68	5.55±0.51	5.61±0.75
Retrocalcaneal bursitis with Achilles' tendinopathy	PRP	7.01±0.85	5.93±0.79	4.86±0.74	3.33±0.97	2.26±0.70
	Steroid	7.10±0.79	6.65±0.99	5.85±0.88	4.85±0.74	3.95±0.75
			FFI score			
Plantar fasciitis	PRP	87.66±4.70	76.66±5.74	57.06±3.45	45.06±3.41	24.66±4.54
	Steroid	89.35±4.59	78.70±4.66	75.25±8.60	71.01±4.65	70.2±6.16
Retrocalcaneal bursitis with Achilles' tendinopathy	PRP	88.33±2.99	75.43±7.93	67.26±5.77	51.26±6.97	38.46±5.96
	Steroid	89.01±5.39	78.55±5.69	73.3±2.75	69.1±5.82	67.75±7.11

Discussion

Use of biological therapy in treatment of various tendinopathy has increased significantly over last 10 years. Clinical improvement was reflected by significant decrease in mean VAS score at every follow up in all forms of injuries. At last follow up mean VAS score indicated a good outcome. Patients who received PRP showed better clinical results (reduction in pain, swelling and improved range of motion) as compared to patients who received steroid. Most of the patients receiving PRP were physiologically relieved and their satisfaction level was higher because of improved functional status as well as relief of local symptoms which led to improved quality of life. No complication related to PRP was observed in our patients.

Small sample size due to limited time of study is a limiting factor for our study. Also patients could have been at different stages of degenerative injury which could not be assessed at the time of enrolment and could have influenced the results.

Ramanan NS et al compared treatment of lateral epicondylitis with PRP or corticosteroid. They found that the group receiving PRP was more often successfully treated than patients treated with corticosteroid. Both group showed improvement in VAS and DASH scores across time, however the scores of corticosteroid group did not show as significant improvement at end of 12 weeks as the PRP group[12]. We had similar observation even after as late as 48weeks. Jeyaraman M et al studied use of autologous PRP to improve functional status and severity of pain around ankle joint by charting VAS and AOFAS (The American Orthopaedic Foot and Ankle Society) score. They too found out improvement in scores on follow up till 6 months[13]. Wang et al. had in demonstrated that treatment of human tenocytes with platelet-rich clot releasate accelerated their proliferation in a dose-dependent manner[14].Reddy et al studied 150 patients with chronic lateral epicondylitis. First group was treated with single injection of corticosteroid, second group was treated with PRP and third group received xylocaine through peppering needle technique. Pain and functional movement were assessed using VAS and Nirschl's staging at 0, 2, 6 12, 26 and 52 weeks. They concluded that PRP, corticosteroid and xylocaine were safe and effective in treatment of lateral epicondylitis. Both steroid and xylocaine were effective on short term period. However on long term follow up, PRP was found out to be more effective treatment with persistent efficacy in relieving pain[15].

Conclusion

It is concluded that autologous PRP is more beneficial than steroid therapy. Use of biologics to improve tissue healing is an ever growing interest in orthopaedics and healing of pathological damage by PRP is more effective method of treatment compared to other modalities and is devoid of significant toxicity. It is cost effective as it does not need expensive equipment and PRP is derived from patient's own blood. However, some patients may not accept the procedure it and some may need multiple injections. Hence the widespread acceptability of the procedure is topic for further research.

Conflict of Interest: None

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