

The Prospective Study on Efficacy and Functional Outcome of Autologous Platelet Rich Plasma Injection in Musculoskeletal Disorders

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Abstract

Background: The musculoskeletal disorders are becoming more common in day to day life due to overuse of tendons and fascia in sedentary individuals. Platelet rich plasma has become a viable, biological and natural healing enhancer and pave a way towards a positive health for musculoskeletal disorders and improve the quality of life. The bioactive materials in platelets induce cellular proliferation, chondrogenesis, angiogenesis and rejuvenation of degenerated tendons and fascia. Platelet rich plasma has decreased the morbidity, accelerates healing and rejuvenation.

Objectives: To evaluate the efficacy and functional outcome of autologous PRP injection in musculoskeletal disorders.

Methods: After screening of cases, 840 cases entered into the study and have been treated with an autologous platelet rich plasma injection with due pre and post procedural care. The cases are followed up pre procedure (day 0) and post procedure at the end of 1st, 3rd and 6th month for pain and range of movements. The patients are followed up for complications and the data were analysed statistically.

Results: There was a significant statistical difference between pre-procedural and post-procedural scoring for each musculoskeletal disorder treated with autologous platelet rich plasma injection. Out of 840 cases, 668 patients (79.52%) reported pain relief with one dose of autologous PRP injection at the end of 1st month follow up and 110 patients (13.09%) reported pain relief after 2nd dose of injection which is given at the interval of 3 weeks from the first dose. No adverse reactions and serious complications were noted in the study participants.

Conclusion: The autologous platelet rich plasma injection is considered superior to other modalities of treatment in musculoskeletal disorders as it provides bioactive micromolecules for tissue rejuvenation.

Keywords: Platelet Rich Plasma; Plantar Fasciitis; Retrocalcaneal Bursitis; Periarthritis; Interscapular Fibrofasciitis; Tennis Elbow; Golfer's Elbow; De Quervain's Tenosynovitis

Introduction

The musculoskeletal disorders are becoming more common in day to day life due to over use of tendons and fascia in sedentary life-style individuals. These musculoskeletal disorders are most common in sports and occupational settings which involve repetitive micro-trauma. Such disorders result in increasing the morbidity by decreasing the functional quality of life of the individual. Platelet rich plasma has become a viable, biological and natural healing enhancer and pave a way towards a positive health for musculoskeletal disorders and improve the quality of life.

Platelet rich plasma, an autologous “Orthobiologic”, is defined as the volume of supernatant containing plasma with platelet concentration of 10^5 - 10^6 above the baseline. The percentage of platelets present in PRP is 94%. Platelet rich plasma is a potent osteogenic and osteointegrative agent [1].

Due to recent advances in molecular biology and regenerative medicine, the induction in the activity of the micromolecules such as bioactive materials and growth factors promotes the improved quality, structure, function and bio-mechanical strength of tissue regeneration and healing process. The bioactive materials in platelets are admixture of pro-angiogenic, anti-angiogenic and chemotactic factor which undergo degranulation and induce cellular proliferation, chondrogenesis, angiogenesis and rejuvenation of degenerated tendons and fascia [2].

Objectives

- The primary objective is to assess the pain scale in terms of VAS score.
- The secondary objective is to evaluate the efficacy and functional outcome of autologous PRP injection in musculoskeletal disorders.

This article optimize the usage and functional outcome of autologous platelet rich plasma in musculoskeletal disorders.

Materials and Methods

- Health care setup: Tertiary care hospital.
- Setting: JJM Medical College, Davangere, Karnataka.
- Duration of the study: June 2016 to May 2018.
- Type of the study: Prospective cohort study.
- Level of evidence: Level IV
- Sample size: 960.
- Selection of cases: 960 cases of musculoskeletal disorders are clinically identified. Among 960 cases, 37 cases failed to satisfy the inclusion criteria, 62 cases lost follow up and 21 cases declined to participate the study. The remaining 840 cases were taken up for this study who were treated with autologous platelet rich plasma injection as per our study protocol.
- Musculoskeletal disorders included in our study are plantar fasciitis, retrocalcaneal bursitis, tennis elbow, golfer’s elbow, de Quervain’s tenosynovitis, periarthrits shoulder and interscapular fibrofasciitis.

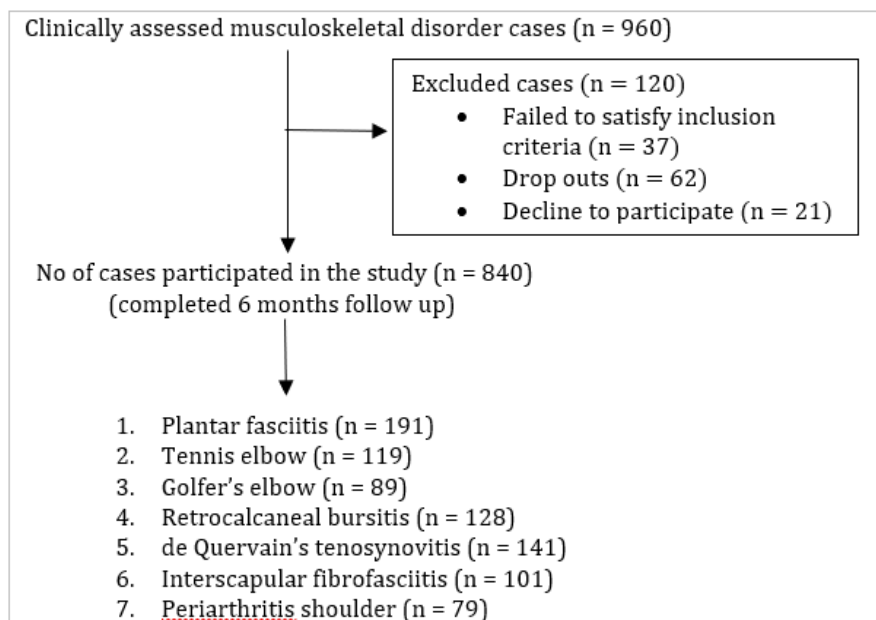


Table 1: Patient’s selection.

Inclusion criteria

1. Patients with plantar fasciitis, tennis elbow, golfer’s elbow, de Quervain’s tenosynovitis, periarthrits shoulder and interscapular fibrofasciitis who have taken conservative treatment without any improvement from past 3 months.
2. Patients with chronic bursitis like retrocalcaneal bursitis who have taken conservative treatment without any improvement from past 3 months.
3. Patients who gave consent for treatment with autologous PRP injection as per our protocol.
4. Regular visits in the out-patient department.

Exclusion criteria

1. Patients with haemoglobin < 10 gm/dL and platelet count < 10^5 / μ L.
2. Patients with corticosteroid injection at treatment site within 1 month.
3. Patients with local infection at the site of the procedure, HIV, Hepatitis B or C, septicaemia and other systemic disorders.
4. Patients refusal for PRP treatment as per our protocol.

After getting IEC clearance from the institute and informed written consent from the patients enrolled in our study, they were subjected for thorough clinical examination and to investigate the duration of the disease and the nature of management taken prior to autologous PRP treatment. The baseline investigations such as complete hemogram, ESR, CRP, renal function tests, random blood glucose, serological testing for HIV 1 and 2 and HbsAg and radiographic analysis of pathological sites were analysed.

Preparation of autologous platelet rich plasma



Placement of citrate and plain vials containing autologous blood samples for differential centrifugation (with counter balance)

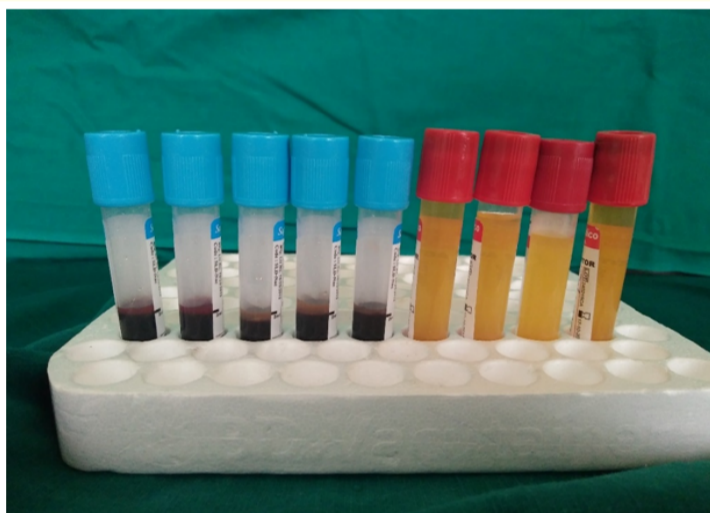


Plate showing citrate vials with RBC layer and plain vials with platelet poor plasma and platelet rich plasma

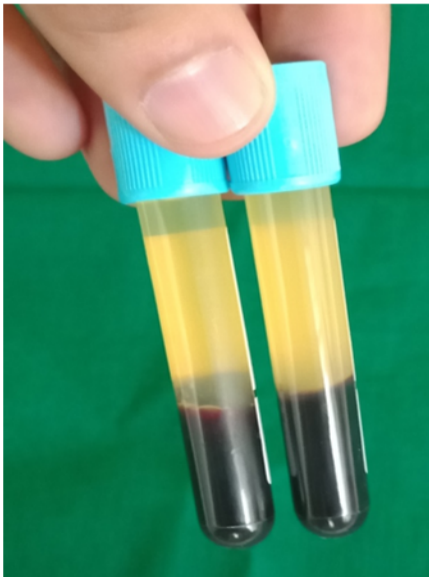

First centrifugation	Second centrifugation
	
<p>Upper 2/3rd portion contain plasma admixed with platelets and buffy coat which contain WBCs and lower 1/3rd portion contain RBCs</p>	<p>Upper 2/3rd portion contain platelet poor plasma (PPP) and lower 1/3rd portion contain platelet rich plasma (PRP)</p>

Figure 1: Preparation of autologous platelet rich plasma injection.

The technique by which autologous platelet rich plasma are called differential centrifugation. With aseptic precautions and the patient in recumbent position, 20 cc of venous blood were drawn in vials containing acid citrate dextrose anticoagulant and subjected for first centrifugation at a rate of 3000 rpm (soft spin) for 10 minutes. Then plasma and buffy coat were separated in the plain tubes which are further subjected for second centrifugation at a rate of 5000 rpm (hard spin) for 10 minutes. The resultant plasma solution contain upper 2/3rd of platelet poor plasma and lower 1/3rd of platelet rich plasma which were withdrawn in the sterile syringes and are injected to the pathological site.

Pre procedural precautions

The cases were investigated for the usage of NSAIDs 72 hours prior and steroids 4 weeks prior to PRP injection. The severity of pain is traced using standard scoring criteria in the pre-procedural period.

Autologous PRP injection technique

With aseptic precautions, the pathological site was painted and draped. Before injecting PRP, calcium chloride was added to PRP in the ratio of 1:10 to activate the platelets. Once calcium chloride have been added into the syringe containing PRP, the syringe was gently mixed for equal distribution of calcium chloride with PRP. After identification of the site of maximum tenderness and without any further delay, the PRP have been injected into the pathological site under ultrasound guidance before PRP coagulate to form a gel. The sterile dressing and crepe bandage were applied at the injection site. The patients were trained for home based strengthening programme.

Post procedural care

All the patients were advised not to bear weight for minimum of 2 weeks and the pain was combated with paracetamol and ice pack application. The patients were followed up for pain and range of movements at the end of 1st, 3rd and 6th month. All patients were followed up for complications and the recorded data were subjected for statistical analysis.

Protocol for disease recurrence

The patients who reported recurrence of symptoms were offered a second dose of autologous PRP injection after 3 weeks of first injection. The time interval of 3 weeks for second dose were due to formation of collagen and proliferation of fibroblasts in the pathological site of the disease process.

Results

The data obtained from the participants of the study were subjected to repeated measures ANOVA test and the following results are obtained.

Disease	Total	Male	Female
Plantar fasciitis	191	112	79
Tennis elbow	119	64	55
Golfer’s elbow	81	47	34
Retrocalcaneal bursitis	128	78	50
de Quervain’s tenosynovitis	141	77	64
Interscapular fibrofasciitis	101	57	44
Periarthritis shoulder	79	47	32
Total no of cases	840	482	358

Table 2: Patients distribution after elimination.

Out of 840 cases, 482 cases (57.38%) were males and 358 cases (42.61%) were females. The mean age of patients participated in our study were 48.48 years with minimum age of 19 years and maximum age of 79 years. All the patients (n = 840) have been given with a single dose of autologous PRP injection after assessing and charting out the pre-procedural functional scoring. Then all the patients were informed to have a follow up in our department for the assessment of pain relief and functional outcome of the autologous PRP injection.

Disease	Total	No of patients cured with 1 st dose of autologous PRP (at end of 1 st month follow up)	No of patients cured with 2 nd dose of autologous PRP	No of patients with recalcitrant disease (at the end of 6 th month follow up)
Plantar fasciitis	191	163	19	9
Tennis elbow	119	97	11	11
Golfer’s elbow	81	67	7	7
Retrocalcaneal bursitis	128	102	15	11
de Quervain’s tenosynovitis	141	109	23	9
Interscapular fibrofasciitis	101	79	14	8
Periarthritis shoulder	79	51	21	7
Total no of cases	840	668	110	62

Table 3: Number of PRP injections.

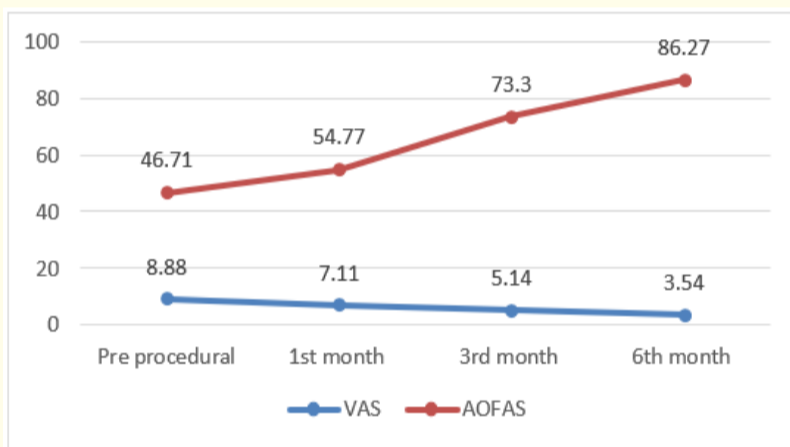
Functional outcome of diseases

Plantar fasciitis

Out of 191 cases of plantar fasciitis, 112 males (58.63%) and 79 females (41.36%) patients got treated with autologous PRP injection. The mean age of patients in plantar fasciitis entity were 55.43 years with minimum age of 26 years and maximum age of 79 years. A total of 163 patients (85.34%) got pain relief with 1st dose of autologous PRP and 19 patients (9.94%) with 2nd dose of injection and 9 patients presented with recalcitrant disease who were counselled for surgical management. The mean pre-procedural VAS and AOFAS scores were 8.88 and 46.71 respectively and the mean post-procedural 6th month VAS and AOFAS scores were 3.54 and 86.27 respectively. A statistically significant improvements were observed in terms of pain relief and functional improvement (p < 0.001).



Image showing autologous PRP injection technique for left plantar fasciitis



Graph 1: Plantar fasciitis.

Tennis elbow

Out of 119 cases of tennis elbow, 64 males (53.78%) and 55 females (46.21%) patients got treated with autologous PRP injection. The mean age of patients in tennis elbow entity were 43.78 years with minimum age of 19 years and maximum age of 77 years. A total of 97 patients (81.51%) got pain relief with 1st dose of autologous PRP and 11 patients (9.24%) with 2nd dose of injection and 11 patients presented with recalcitrant disease who were counselled for surgical management. The mean pre-procedural VAS and Mayo’s elbow scores were 8.84 and 42.20 respectively and the mean post-procedural 6th month VAS and Mayo’s elbow scores were 3.56 and 83.85 respectively. A statistically significant improvements were observed in terms of pain relief and functional improvement ($p < 0.001$).

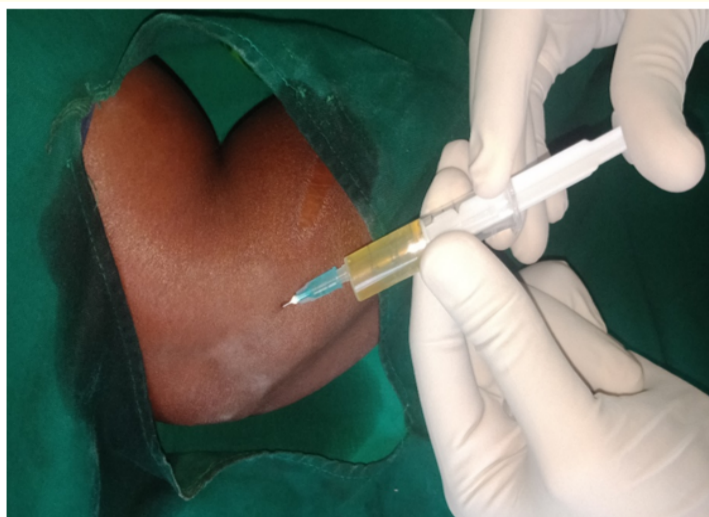
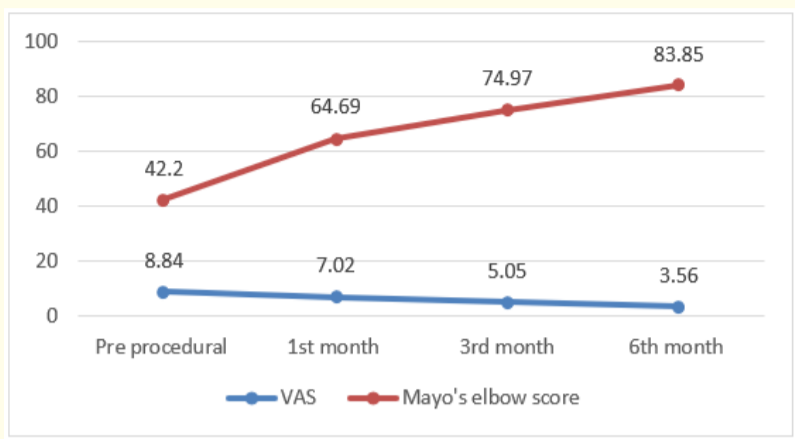


Image showing autologous PRP injection technique for right tennis elbow



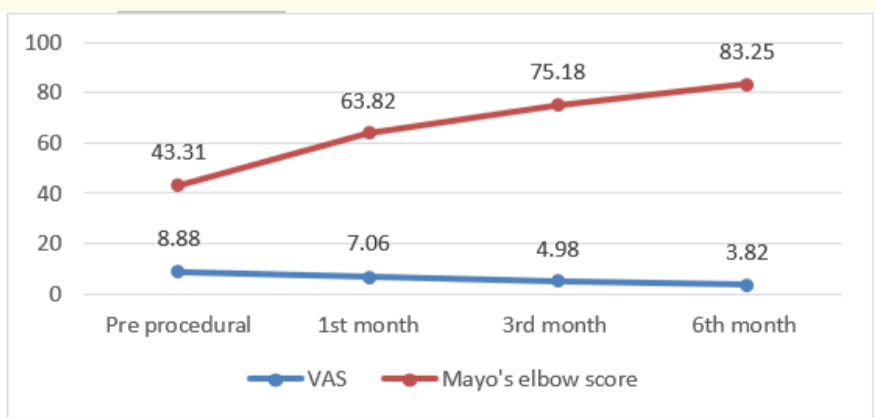
Graph 2: Tennis elbow.

Golfer's elbow

Out of 81 cases of golfer's elbow, 47 males (58.02%) and 34 females (41.97%) patients got treated with autologous PRP injection. The mean age of patients in golfer's elbow entity were 44.87 years with minimum age of 24 years and maximum age of 68 years. A total of 67 patients (82.71%) got pain relief with 1st dose of autologous PRP and 7 patients (8.64%) with 2nd dose of injection and 7 patients presented with recalcitrant disease who were counselled for surgical management. The mean pre-procedural VAS and Mayo's elbow scores were 8.88 and 43.31 respectively and the mean post-procedural 6th month VAS and Mayo's elbow scores were 3.82 and 83.25 respectively. A statistically significant improvements were observed in terms of pain relief and functional improvement ($p < 0.001$).



Image showing autologous PRP injection technique for right golfer's elbow



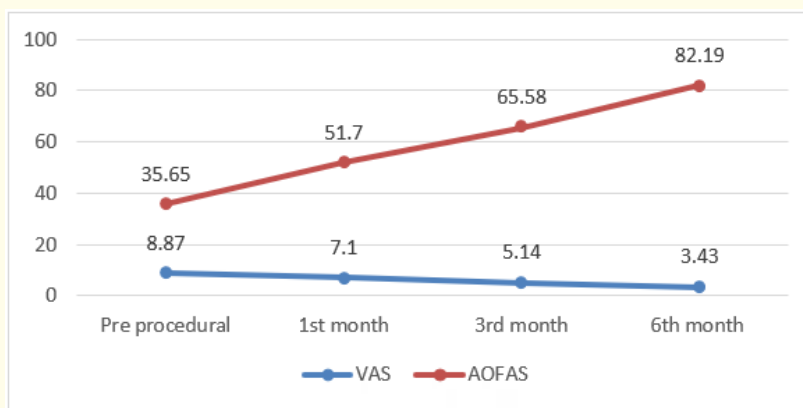
Graph 3: Golfer's elbow.

Retrocalcaneal bursitis

Out of 128 cases of retrocalcaneal bursitis, 78 males (60.93%) and 50 females (39.06%) patients got treated with autologous PRP injection. The mean age of patients in retrocalcaneal bursitis entity were 51.15 years with minimum age of 32 years and maximum age of 69 years. A total of 102 patients (79.68%) got pain relief with 1st dose of autologous PRP and 15 patients (3.90%) with 2nd dose of injection and 11 patients presented with recalcitrant disease who were counselled for surgical management. The mean pre-procedural VAS and AOFAS scores were 8.87 and 35.65 respectively and the mean post-procedural 6th month VAS and AOFAS scores were 3.43 and 82.19 respectively. A statistically significant improvements were observed in terms of pain relief and functional improvement ($p < 0.001$).



Image showing autologous PRP injection technique for left retrocalcaneal bursitis



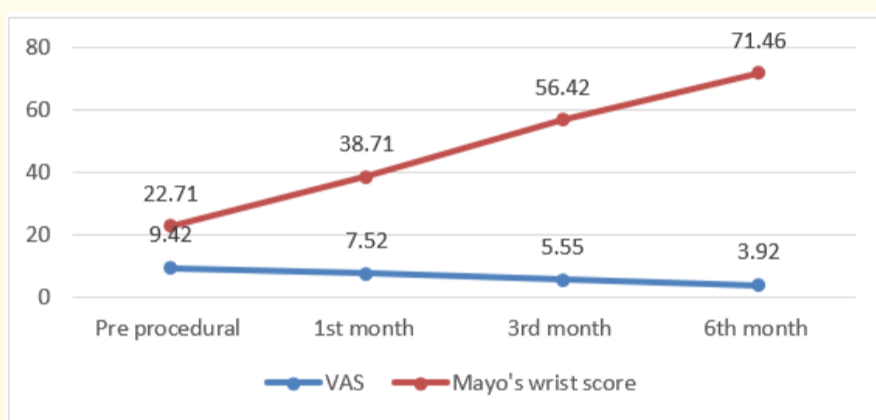
Graph 4: Retrocalcaneal bursitis.

de Quervain’s tenosynovitis

Out of 141 cases of de Quervain’s tenosynovitis, 77 males (54.60%) and 64 females (45.39%) patients got treated with autologous PRP injection. The mean age of patients in de Quervain’s tenosynovitis entity were 41.24 years with minimum age of 21 years and maximum age of 59 years. A total of 109 patients (77.30%) got pain relief with 1st dose of autologous PRP and 23 patients (16.31%) with 2nd dose of injection and 9 patients presented with recalcitrant disease who were counselled for surgical management. The mean pre-procedural VAS and Mayo’s wrist scores were 9.42 and 22.71 respectively and the mean post-procedural 6th month VAS and Mayo’s wrist scores were 3.92 and 71.46 respectively. A statistically significant improvements were observed in terms of pain relief and functional improvement ($p = 0.001$).



Image showing autologous PRP injection technique for left de Quervain's tenosynovitis



Graph 5: de Quervain's tenosynovitis.

Interscapular fibrofasciitis

Out of 101 cases of interscapular fibrofasciitis, 57 males (56.43%) and 44 females (43.56%) patients got treated with autologous PRP injection. The mean age of patients in interscapular fibrofasciitis entity were 52.51 years with minimum age of 29 years and maximum age of 70 years. A total of 79 patients (78.21%) got pain relief with 1st dose of autologous PRP and 14 patients (13.86%) with 2nd dose of injection and 8 patients presented with recalcitrant disease who were counselled for surgical management. The mean pre-procedural VAS and DASH scores were 9.01 and 77.31 respectively and the mean post-procedural 6th month VAS and DASH scores were 3.81 and 32.40 respectively. A statistically significant improvements were observed in terms of pain relief and functional improvement ($p = 0.002$).

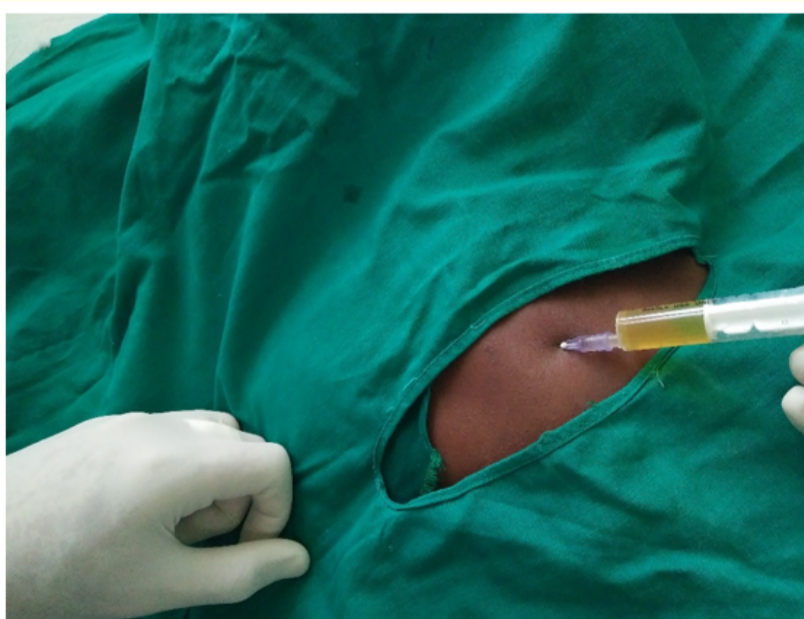
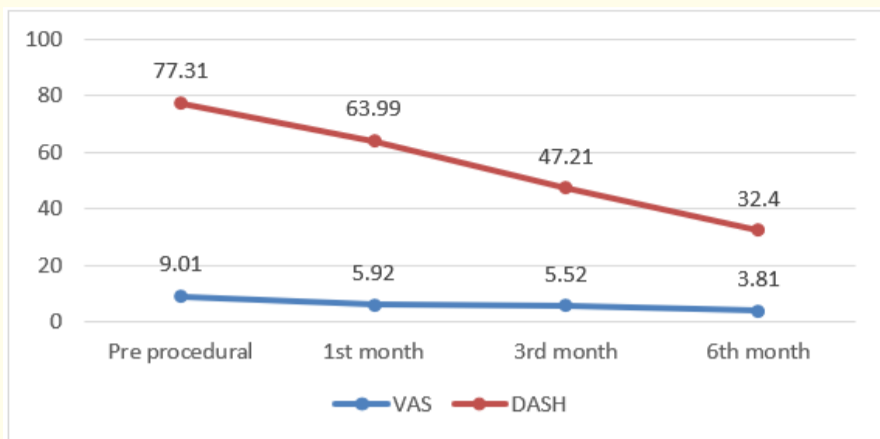


Image showing autologous PRP injection technique for left interscapular fibrofasciitis



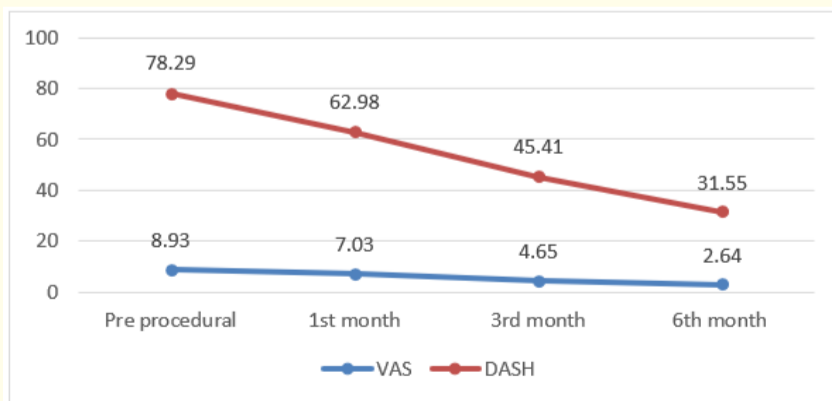
Graph 6: Interscapular fibrofasciitis.

Periarthritis shoulder

Out of 79 cases of periarthritis shoulder, 47 males (59.49%) and 32 females (40.50%) patients got treated with autologous PRP injection. The mean age of patients in periarthritis shoulder entity were 50.52 years with minimum age of 34 years and maximum age of 66 years. A total of 51 patients (64.55%) got pain relief with 1st dose of autologous PRP and 21 patients (26.58%) with 2nd dose of injection and 7 patients presented with recalcitrant disease who were counselled for surgical management. The mean pre-procedural VAS and DASH scores were 8.93 and 78.29 respectively and the mean post-procedural 6th month VAS and DASH scores were 2.64 and 31.55 respectively. A statistically significant improvements were observed in terms of pain relief and functional improvement ($p < 0.001$).



Image showing autologous PRP injection technique for right periarthritis shoulder



Graph 7: Periarthritis shoulder.

Disorder	Scoring	Repeated measures ANOVA test (p value)			
		Pre procedure	Post procedure		
			1 st month	3 rd month	6 th month
Plantar fasciitis (n = 191)	VAS	0.527	0.045	0.001	< 0.001
	AOFAS	0.671	0.091	0.006	< 0.001
Tennis elbow (n = 119)	VAS	0.415	0.021	0.003	< 0.001
	Mayo's elbow score	0.087	0.056	0.026	< 0.001
Golfer's elbow (n = 89)	VAS	0.456	0.314	0.001	< 0.001
	Mayo's elbow score	0.077	0.034	0.012	< 0.001
Retrocalcaneal bursitis (n = 128)	VAS	0.763	0.173	0.024	0.041
	AOFAS	0.537	0.287	0.060	< 0.001
de Quervain's tenosynovitis (n = 141)	VAS	0.691	0.274	0.001	< 0.001
	Mayo's wrist score	0.213	0.091	0.005	0.001
Interscapular fibrofasciitis (n = 101)	VAS	0.647	0.231	0.053	0.004
	DASH	0.715	0.078	0.031	0.002
Periarthritis shoulder (n = 79)	VAS	0.731	0.199	0.063	0.002
	DASH	0.412	0.110	0.006	< 0.001

Table 4: p value of repeated measure ANOVA test.

Out of 840 cases, 668 patients (79.52%) reported pain relief with one dose of autologous PRP injection at the end of 1st month follow up and 110 patients (13.09%) reported pain relief after 2nd dose of injection which is given at the interval of 3 weeks from the first dose. 62 patients (7.38%) presented with recalcitrant disease after 6 months of first dose. Overall our study showed a statistically significant difference between pre-procedural and post-procedural scores in subjective (VAS) and functional (AOFAS, Mayo wrist score, Mayo elbow score and DASH) scoring system. The patients who took autologous PRP injection showed a statistically significant (p < 0.05) improvement in combating all seven musculoskeletal disorders included in the study.

Table 5: Complications.

Disease	Pain	Swelling	Recurrence
Plantar fasciitis	77	19	9
Tennis elbow	41	15	11
Golfer's elbow	29	12	7
Retrocalcaneal bursitis	19	7	11
de Quervain's tenosynovitis	24	7	9
Interscapular fibrofasciitis	9	3	8
Periarthritis shoulder	11	7	7
Total no of cases	210	70	62

The complications found in our patients were pain at the injection site in 210 cases (25%), swelling in 70 cases (8.33%) and recurrence of symptoms in 62 cases (7.38%). No other adverse reactions noted in the patients participated in the study. All 62 recalcitrant cases are counselled for surgical management.

Discussion

Musculoskeletal disorders are most common among sports and occupational settings due to over usage and repetitive microtrauma over bone tendon junction and fascia & sheaths covering musculotendinous units[3]. Over usage syndrome describes the painful conditions affecting tendons associated with repetitive strain, overuse, ageing, degeneration, or poor biomechanics. These musculoskeletal disorders worsen the quality of life by causing pain and impairing mobility, decreasing the ability to perform daily activities, and compromising an active lifestyle[4].

Management options for musculoskeletal disorders

- A) Non pharmacological management[3]
 - o PRICE model – Protection, Rest, Ice application, Compression & Elevation
 - o POLICE model – Protection, Optimal Loading, Ice application, Compression & Elevation

- B) Pharmacological management[4,5]
 - Analgesics and muscle relaxants,
 - Local steroid infiltration in the form of 40 mg of triamcinolone into the affected tendon sheath which reduces inflammation,
 - Local sodium hyaluronate injection, which act as a viscosupplement by increasing the viscosity of the synovial fluid, which helps to lubricate, cushion and reduce the pain
- C) Physical therapy[4,5]
 - Active range of affected joint movements, ultrasonic therapy and soft tissue massage of the affected joints,
 - Home based exercise programme in the form of hot fomentation and active range of movement exercises,
 - Orthotics like braces and splints which reduce the micromotion at the injured area
- D) Biological therapy[1,2,6]
 - Loco-regional cryotherapy with -110 °C to -140 °C provides anti-inflammatory and analgesic effect to the degenerated tendon sheath
 - Autologous platelet rich plasma (PRP) injection, homologous platelet lysate (HPL) injection
 - Tissue bioengineering with mesenchymal stem cell and silk scaffolds, autologous tenocyte injection and injection of microRNA.
- E) Surgical therapy[7,8]
 - Open or arthroscopic release of fibrosis of tendon sheath covering tendons
 - Ultrasound guided percutaneous needle tenotomy of the affected tendon sheath
- F) Future treatment modalities
 - Local or intra-articular collagenase injections which breaks down the peptide bonds in collagen
 - Biological agents of anti-TNF agents are under clinical research.

In this article, we considered autologous platelet rich plasma injection for musculoskeletal disorders as per our protocol.

Platelet rich plasma

Platelet rich plasma, an autologous “Orthobiologic”, is defined as the volume of supernatant containing plasma with platelet concentration of 10^5 - 10^6 above the baseline. The percentage of platelets present in PRP is 94%. Platelet rich plasma is a potent osteogenic and osteointegrative agent[1,2].

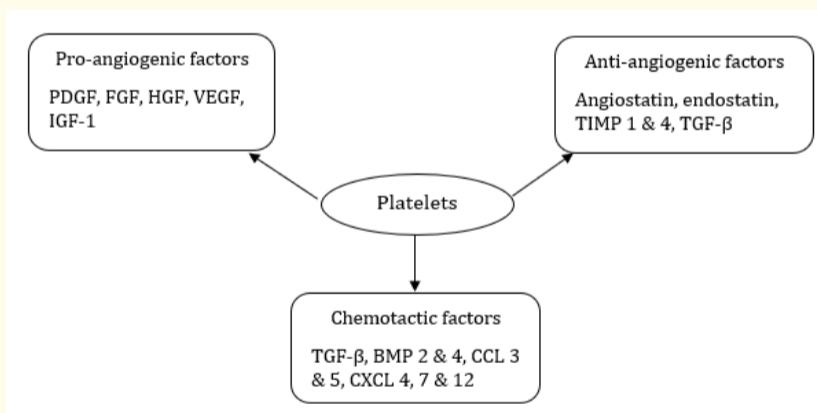


Figure 2: Factors present in platelets.

The rationale behind platelet rich plasma in management of musculoskeletal disorders are due to the interplay between histopromotive factors such as pro-angiogenic, anti-angiogenic and chemotactic factors present in platelets. The binding of growth factor to target cell receptor induces a signal transduction mechanism which produces a biological response for chemotaxis, cell proliferation and osteoblastic differentiation. The molecular basis of platelet rich plasma is due to increased HGF and TNF- α activity by disrupting NF- κ B-transactivating activity [9,10,11,12].

Growth factors in PRP[9,10]

Growth factors are polypeptide dimers with 2 antiparallel monomers arranged in cystine knot configuration where cystine acts as an ability for disulphide bonding between monomer chains. Growth factors acts through tyrosine kinase receptor pathway by dimerization through ligand bonding. It leads to tyrosine autophosphorylation between paired intracellular tails which further catabolize to phosphorylate other growth factors and intracellular proteins. Finally, it enters transcription, translation, cell division and migration.

Growth factors	Significance
Platelet derived growth factor (PDGF)	<ul style="list-style-type: none"> • Potent cellular mitogen, migration, proliferation and matrix synthesis • Stimulates the production of proteoglycans, hyaluronate, collagen and fibronectin • Induction of angiogenesis • Induction of osteoplastic, osteoclastic and regulatory effects on bone formation
Transforming growth factor β (TGF- β)	<ul style="list-style-type: none"> • Potent inducer of collagen type-1 synthesis, angiogenesis and wound contraction • Proliferation of fibroblasts • Pleotropic shift to myofibroblasts • Maintains cartilage matrix composition and intrinsic repair • Possess anti-inflammatory and immunosuppressive effects
Vascular endothelial growth factor (VEGF)	<ul style="list-style-type: none"> • Promotes neoangiogenesis • Enhances endothelial cell mitogenicity • Increases metalloproteinase activity
Fibroblast growth factor (FGF)	<ul style="list-style-type: none"> • Promotes cellular growth and collagen type – 1 production • Induces fibroblast proliferation and regeneration of tissues
Epidermal growth factor (EGF)	<ul style="list-style-type: none"> • Induces regeneration of epidermal cells • Promoter of wound healing by keratinocyte proliferation • Enhancer of production of growth factors • Triggers EGF-R for DNA synthesis and cellular proliferation
Insulin like growth factor-1 (IGF-1)	<ul style="list-style-type: none"> • Chemotactic for fibroblasts • Stimulator for protein synthesis • Proliferation and differentiation of osteoblasts

The phases of activated PRP follows four phases namely [9].

- Inflammatory phase is characterized by increased vascular permeability, initiation of angiogenesis, stimulation of tenocyte proliferation and initiation of type III collagen synthesis over injection site which lasts for 48 – 72 hours
- Proliferative phase is characterized by accumulation of fibroblast proliferation and neoangiogenesis which lasts from 1 to 6 weeks. During this phase, water content and glycosaminoglycan concentration remains high.
- Remodelling phase commences approximately after 6 weeks and lasts till 10 weeks with decreased cellularity and decreased collagen and glycosaminoglycan synthesis
- Maturation phase is characterized by synthesis of type I collagen which lasts from 10 weeks to 6 months. In this phase, the metabolism of tenocyte remains high.

If the patient recurs with symptoms, the next dose of PRP injection should be given with an interval of 3 weeks. The time duration of 3 weeks is provided for the initiation of fibroblast proliferation and neoangiogenesis.

Deepak Chaudhary, *et al* studied the functional outcome and results of PRP in treatment of delayed union of fractures in 6 patients. About 83.3% of delayed union patients achieved union after thrice weekly autologous injection of PRP at fracture site for 4 weeks while in 16.6% cases progressed to non union which was treated by revision surgery with autologous cancellous bone grafting [13].

Bielecki T, *et al* studied the benefit of percutaneous injections of Autologous Platelet Leucocyte Rich Gel (PLRG) in 15 delayed and 22 non-union cases. In delayed union group, all cases achieved union in 9.3 weeks. In non-union group, the union was observed in 13 of 20 cases with time of 10.3 weeks. In 2 patients, destabilization of fracture occurred after 5 months. In 4 cases, bone healing processes were not observed inspite of prolonged observation. In one patient, union did not occur and there was a mass of callus in the fracture site [14].

Peerbooms JC, *et al* conducted a RCT with 100 patients of 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. According to VAS, 24 of the 49 patients (49%) in the corticosteroid group and 37 of the 51 patients (73%) in the PRP group were successful, which was significantly different ($P < 0.001$) [15].

Randelli PS, *et al* conducted an uncontrolled pilot study of PRP augmentation along with arthroscopic rotator cuff repair in 14 patients. They reported statistically significant improvements in VAS and UCLA shoulder scores compared to preoperative values. They reported that autologous PRP reduced pain in the first postoperative month and that the long term results of subgroups of grade 1 and 2 tears suggested that PRP positively affected cuff healing [16].

Filardo G, *et al* evaluated the efficacy of PRP injections for refractory patellar tendinopathy on 15 cases Vs 16 controls which showed statistically significant improvement in Tegner, EQ VAS and pain level at the end of PRP injections and a further improvement was noted at six months and concluded that PRP injections had the potential to promote the achievement of a satisfactory clinical outcome, even in chronic patellar tendinopathy [17].

Martin J., *et al* conducted a retrospective study on PRP for Chronic Plantar Fasciitis in 23 patients. FAOS, SF-12 and VAS scores were collected at a minimum of 6 months follow-up. The mean VAS score improved from 7 to 4. The pain, symptoms, and quality of life subscales of the FAOS and SF-12 significantly improved from preinjection scores. Five patients went on to have endoscopic release of the plantar fascia at an average of 94 days after the last injection. Six patients obtained full resolution of symptoms while the majority of patients were able to forgo surgery due to improvement from the PRP injection [18].

DeJonge S., *et al* studied an one year follow up of platelet rich plasma treatment in chronic Achilles tendinopathy: A double blind randomized placebo controlled trial. Studied 44 patients with chronic tendinopathy 2–7 cm proximal to the Achilles tendon insertion and injected them with PRP or saline and subjected the patients to an eccentric training program and followed up for 6, 12 & 24 weeks and 1 year. One year of follow up showed no clinical and ultrasonographic superiority of PRP injection over the placebo injection [19].

Venkatesh Gupta, Divya Bandari conducted a study on autologous platelet rich plasma injection in 60 cases of tennis elbow and 40 cases of plantar fasciitis. The results of autologous PRP injection has been evaluated with VAS, DASH and FHSQ scoring system. Both group of patients were clinically and functionally evaluated after 4th and 8th week of initial PRP injection which showed statistically significant improvement in pain and quality of life [20].

Jose I Martin., *et al* studied the role of Platelet-rich plasma (PRP) in chronic epicondylitis: study protocol for a randomized controlled trial. 80 patients were allocated to have ultrasound guided needling combined with a leukocyte-depleted PRP or lidocaine each alternate week for a total of two interventions. The primary outcome measure is assessed by changes in pain and activity levels, as calculated by DASH score, at 6 months. Secondary outcome measures include changes in DASH at 3 and 12 months, changes in pain as assessed by the visual analogue scale (VAS) at the 6 weeks, 3, 6, and 12 months follow-up. Potential efficacy analysis will be performed as intention to treat, comparing the percentage of patients that have achieved therapeutic success in each group using the chi-squared test with $P < 0.05$ deemed statistically significant [21].

Ankit Varshney, *et al* conducted a randomized study on autologous platelet-rich plasma versus corticosteroid in the management of elbow epicondylitis in 83 patients. 50 cases in group A received corticosteroid injection and 33 cases in group B received autologous PRP injection. At the end of 6 months, cases who received PRP injections showed a significant improvement in VAS ($p < 0.05$) and MAYO ($p < 0.05$) in contrast with steroid group whereas no statistical difference was found between the two groups at 1 and 2 months after intervention [22].

Shashank Yeshwant Kothari, *et al* studied the efficacy of PRP injection, corticosteroid injection and ultrasonic therapy for periarthritis shoulder. Patients with periarthritis shoulder ($n=195$) were randomised to receive single injection of PRP (2 ml) or corticosteroid (80 mg of methylprednisolone) or ultrasonic therapy (seven sittings in two weeks). Participants were evaluated at 0, 3, 6 and 12 weeks. PRP treatment resulted in statistically significant improvements over corticosteroid and ultrasonic therapy in active as well as passive range of motion of shoulder, VAS and QuickDASH at 12 weeks. At six weeks, PRP treatment resulted in statistically significant improvements over ultrasonic therapy in VAS and QuickDASH. No major adverse effects were observed [23].

Aslani H., *et al* conducted an experimental PRP therapy for frozen shoulder in a volunteer revealed 2 consecutive doses of PRP with an interval of 4 weeks improved functional range of movements and pain relief. He emphasised 2-fold improvement for range of movements with PRP therapy [24].

In this article, we considered autologous platelet rich plasma injection for musculoskeletal disorders for those above mentioned clinical entities. Our study show the functional improvement in 668 patients with 1st dose of autologous PRP injection and 110 patients with 2nd dose of autologous PRP injection with an interval of 3 weeks from the first dose and presented with statistically significant results with p value < 0.001 .

Autologous platelet rich plasma injection offer advantages of increased bioactive micromolecules at the injured or diseased site, provides a scaffold or framework for the healing process, elimination of disease transmission and immunological concern and the biological modality of treatment for musculoskeletal disorders. Platelet rich plasma provide a high margin of therapeutic efficacy and safety.

Limitation

- Further research on the natural history of musculoskeletal disorders has to be evaluated which will guide the researchers to target the micromolecules which prevents the degeneration of soft tissues and improve the functional quality of life.
- Standardization of PRP injection protocol has to be figured out.

Conclusion

The autologous platelet rich plasma injection is considered superior to other modalities of treatment in musculoskeletal disorders as it provide bioactive micromolecules for tissue rejuvenation. The platelet rich plasma became a potential tool in tissue engineering and regenerative medicine. A further research on bioactive micromolecules have to be conducted to evaluate the potency, credibility and temporal association of musculoskeletal disorders with improved quality of life and long term outcome.

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