



A Randomized Controlled Study to Evaluate the Effectiveness of Local Platelet Rich Plasma (PRP) Injection for the Management of the Cases of Planter Fasciitis - Final Outcome of 179 Cases at 12 Months

KEYWORDS

Platelet Rich Plasma, planter fasciitis, heel pain, local infiltration, autologous PRP

Prof S.P.S. Gill

Professor & HOD Dept Of Orthopaedics, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, UP

Dr Jasveer Singh

Assistant Professor Dept Of Orthopaedics, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, UP

Dr Manish Raj

Assistant Professor Dept Of Orthopaedics, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, UP

Dr Pulkesh Singh

Assistant Professor Dept Of Orthopaedics, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, UP

Dr Ankit Mittal

Assistant Professor Dept Of Orthopaedics, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, UP

Dr Rakesh Vishwakarma

Resident, Dept Of Orthopaedics, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, UP

ABSTRACT Introduction

Planter fasciitis is an inflammation of the plantar fascia at the bottom of the foot. Though pathology of plantar fasciitis remains ill understood, there is evidence to suggest that it is probably initiated by repeated micro trauma. Numerous methods have been advocated for treating plantar fasciitis, including rest, NSAID's, night splints, foot orthosis, stretching protocols and ESWT (extra corporeal shock wave therapy), local laser application, autologous blood injection and local ultrasound application. Platelet rich plasma (PRP) is promoted as an ideal autologous biological blood-derived product, which can be exogenously applied to various tissues where it releases high concentrations of platelet derived growth factors that enhance wound healing, bone healing and also tendon healing. In current study evaluate the effectiveness of local infiltration of autologous platelet rich plasma (PRP) and compared the results with control group.

Method

Present study conducted in department of orthopedics of a tertiary level 1000 bedded Super specialty Medical College situated in rural area of North India. Cases were selected from the patients attending routine OPD from January 2007 to December 2015 at orthopedics department. 10 ml of a patient's own blood was collected via blood draw, maintaining sterile technique, with SYRINGE and then mixed with 2 ml Acid citrate dextrose (anticoagulant). This was then put in Autologous Platelet Separator System (1500 RPM for 5 minutes), yielding platelet rich plasma (PRP) as supernatant. Under sterile conditions, patients were receiving a 3 cc PRP injection (consisting of their own PRP) into the origin of the plantar fascia and site of maximum tenderness. We followed up patients at 2 weeks, 4 weeks, 8 weeks, 12 weeks and final at 52 weeks. The results tabulated as per the Performa. We used visual analogue scale (VAS) for assessment of pain relief in two groups.

Results

At the start of study the mean VAS of control group was 6.5 and mean VAS of case group (PRP) was 6.6. The mean VAS score in case group (PRP) decreases from baseline 6.6 at start to 0.54 at 52 wk during follow up. We noticed that there was maximum decrease in mean VAS score in case group from first week (VAS-6.6) to 12 weeks (VAS-1.7). We concluded that PRP injection at planter fasciitis site have much better outcome in relation to visual analogue score(VAS) and result difference was statistically significant.

Conclusion

Planter fasciitis is a very disabling disorder of foot leaving to very discomforting life and day to activity. Autologous platelet rich plasma (PRP) infiltration at the most tender part of heel is a effective method of management of these cases as compared to conservative management. This method also shown negligible complication rate and low recurrence rate. Conservative management of these cases had shown poor long term results.

Introduction

Planter fasciitis is an inflammation of the plantar fascia at the bottom of the foot. Heel spurs are soft, bendable deposits of the calcium that are result of the tension and inflammation at the plantar fascial attachment to the calcaneum¹

Though pathology of plantar fasciitis remains ill understood, there is evidence to suggest that it is probably initiated by repeated micro trauma. The inflammation is never acute and in chronic cases, in fact, that there is a loss of inflammatory response & chronic scar formation.^{2,3,4}

Numerous methods have been advocated for treating plantar fasciitis, including rest¹, NSAID's², night splints, foot

orthosis, stretching protocols^{3,4,5} and ESWT (extra corporeal shock wave therapy)^{6,7}, local laser application⁸, autologous blood injection⁹ and local ultrasound application^{10,11}. Steroid injections are a popular method of treating the condition but only seem to be useful in the short term and only to a small degree. The use of corticosteroids has been linked to rupture of plantar fascia especially after repeated local injections^{12,13,14}. Various types of surgical procedures have also been recommended for refractory cases.

Platelet rich plasma (PRP)^{15,16,17} is promoted as an ideal autologous biological blood-derived product, which can be exogenously applied to various tissues where it releases high concentrations of platelet derived growth factors that enhance wound healing, bone healing and also tendon

healing. In addition, PRP possesses antimicrobial properties that may contribute to the prevention of infections^{18,19}. When platelets become activated, growth factors are released and initiate the body's natural healing response. Injection of these platelets in the attachment of the fascia to the os calcis might induce a healing response^{20,21,22}.

Platelets were initially known to be responsible for blood clotting. In the last 20 years we have learned that when activated in the body, platelets release healing proteins called growth factors.

There are many growth factors with varying responsibilities, however cumulatively they accelerate tissue and wound healing.

PRP is promoted as an ideal autologous biological blood-derived product, which can be exogenously applied to various tissues where it releases high concentrations of platelet derived growth factors that enhance wound healing, bone healing and also tendon healing¹². In addition PRP possesses antimicrobial properties that may contribute to the prevention of infections. When platelets become activated, growth factors are released and initiate the body's natural healing response.

The use of platelet rich plasma (PRP) injections in the treatment of plantar fasciitis is a fairly recent and evolving concept. The injection of platelet-rich-plasma (PRP) into the affected tissue addresses the healing stages necessary to reverse the degenerative process which are going on in the base of the plantar fascia. PRP injections are very effective in chronic cases where steroids usually do not work.

The individual cytokines present in the platelet-granules have been shown to enhance fibroblast migration and proliferation, up-regulate vascularization, and increases collagen deposition in a variety of in vitro and in vivo setting. The cytokines present in platelet-granules have been shown to affect the healing stages necessary to reverse a chronic plantar fasciitis condition. Additionally, many of these cytokines have been seen to work in a dose dependent manner. [Table 1]

Table 1-Function of different growth factor released by platelets on MUSCULOSKELETAL SYSTEM²³

PDGF	Mitogenetic for mesenchymal and osteoblastic cells; osteo inductive; regulates collagenase secretion and collagen synthesis' 27-29
TGF-	Stimulates undifferentiated mesenchymal cell proliferation; regulates fibroblastic and osteoblastic mitogenesis; regulates collagen synthesis and collagenase secretion; stimulates endothelial chemotaxis and angiogenesis ^{27,30-32}
FGF-	Promotes growth and differentiation of chondrocytes and osteoblasts; mitogenetic effect on mesenchymal, chondrocytes and osteoblasts cell ^{33,34}
IGF 1	Play a role in bone remodeling and mineralization 35,36
IGF 2	Stimulates proliferation of osteoblast-like cells; promote collagenous protein synthesis 37,38
VEGF-	Increases angiogenesis and vessel permeability, stimulates mitogenesis of endothelial cells -39
EGF-	Stimulates endothelial chemotaxis/angiogenesis; regulates collagenase secretion; stimulates epithelial/mesenchymal mitogenesis 40,41
IL-8	Promotes osteoclast formation as well as angiogenesis 42,43

CTGF-	Promotes angiogenesis, cartilage regeneration, fibrosis and platelet adhesion 44,45
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PDGF: Platelet-derived growth factor, **TGF- :** Transforming growth factor beta, **FGF:** Fibroblast growth factor, **VEGF:** Vascular endothelial growth factor, **IGF;** Insulin like growth factors

Material And Method

Present study conducted in department of orthopedics of a tertiary level 1000 bedded Super specialty Medical Collage situated in rural area of North India. Cases were selected from the patients attending routine OPD from January 2007 to December 2015 at orthopedics department.

Patient presenting with pain at the bottom of the heel especially severe in the morning and on initial few steps after period of prolonged rest were selected for this study.

Diagnosis were made mainly on clinical grounds i.e. on palpation there was mild to severe tenderness on medial calcaneum tubercle and sometimes on lateral aspect of heel. All patients between 18 to 60 yrs were considered in this prospective randomized controlled trial.

All patients evaluated for age, sex, bilateralism, duration of symptoms, time of the day when there was maximum pain, type of pain, location of maximum tenderness in the foot, any specific aggravating factor, associated conditions and any previous history of steroid injections.

Eligibility

Ages Eligible for Study:	18 Years to 60 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Inclusion Criteria:

Patients presenting with complaints of plantar heel pain, worse with rising in morning and/or after periods of sitting or lying presenting for at least 4 weeks

Examination reveals maximal tenderness at the attachment of the plantar fascia on the medial tubercle of the calcaneum

Willingness to participate in an investigational technique

Willingness to forgo any other concomitant conservative treatment modality; NSAIDS and orthotic devices during the study period

Exclusion Criteria

Previous surgery for heel pain

Nerve related symptoms (radiculopathy, tarsal tunnel syndrome, tarsi sinus syndrome)

Patient with complex regional pain syndrome

Achilles tendon pathology

RA, DM, local or systemic infection, PVD, metabolic disease such as gout, clotting disorder, anticoagulation therapy

Patients that are pregnant or breastfeeding

Patients with metastatic cancer

Dysfunction of the knee, ankle, or foot

Work related or compensable injury

Previous treatment: corticosteroid injection in the last 6 months or NSAIDs treatment within the last 7 days

We divided our patients in two groups randomly using simple number randomizing method. Study design for this study was randomized case control study.

GROUP A- These patients were treated with Conservative method like soft heel pads, NSAIDs, local warm fomentation.

GROUP B- These patients were treated with autologous platelet rich plasma injections plus conservative methods as of Group A

10 ml of a patient's own blood was collected via blood draw, maintaining sterile technique, with SYRINGE and then mixed with 2 ml Acid citrate dextrose (anticoagulant). This was then put in Autologous Platelet Separator System (1500 RPM for 5 minutes), yielding platelet rich plasma (PRP) as supernatant. [Figure 1]

Figure 1- Blood after centrifugation



A site of maximum tenderness was pre-marked with a sterile marker. Under sterile conditions, patients were receiving a 3 cc PRP injection (consisting of their own PRP) into the origin of the plantar fascia and site of maximum tenderness. [Figure 2] A peppering technique spreading in clockwise manner used to achieve a more expansive zone of delivery, with a maximum of 10 passes through the fascia itself. The patient was monitored for 10 minutes in OT for adverse reactions. Autologous Platelet rich plasma 3 ml injected at the site of maximum tenderness under sterile conditions followed by local conservative management like Soft heel pads, local warm application

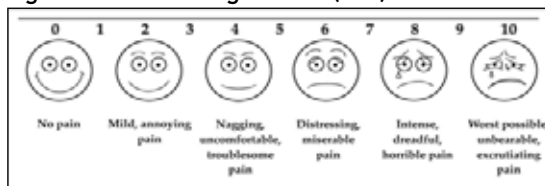
and systemic NSAIDs. Local 2% Lignocaine was injected beforehand.

Figure 2- Infiltration of heel with PRP



We followed up patients at 2 weeks, 4 weeks, 8 weeks, 12 weeks and final at 52 weeks. The results tabulated as per the Performa. We used visual analogue scale (VAS) for assessment of pain relief in two groups. [Figure 3]

Figure 3- Visual analogue score (VAS)



Results-

The study comprises of a total of 179 patients (93 male 86 female) of chronic planter fasciitis treated from 2007 to 2014. Out of 179 cases 91 cases were kept in cases group and 88 cases were kept in control group. Patients were the age group of 18-60. The youngest patients was a boy 18 yr old male and oldest was 58 yr old female. The mean patients age 41.31 yr in Case group (20-58) and 42.10 yr for control group. Duration of pain was more than 6 month on average. Bilateral planter fasciitis found in 30% cases. Calcaneum spur was associated with flat foot in 20 patients. 20% patients were associated with high arched foot with narrow weight bearing heel surface.

Patients were followed up at 2, 4, 8, and 12 weeks and final at 52 weeks. We used (VAS) visual analogue score for assessment of pain relief in both cases and control groups. At the start of study the mean VAS of control group was 6.5 and mean VAS of case group (PRP) was 6.6. The mean VAS score in case group (PRP) decreases from baseline 6.6 at start to 0.54 at 52 wk during follow up. [Table 2] We noticed that there was maximum decrease in mean VAS score in case group from first week (VAS-6.6) to 12 weeks (VAS-1.7). Maximum symptomatic improvements were seen in first 12 weeks of the PRP injection. In control groups the mean VAS at the start of study was 6.5 and at 12 weeks we able to achieve VAS up to 5.9 only with conservative management without any PRP injection. [Table 3] After 12 weeks there was gradual increase in mean VAS from 5.9 at 12 weeks to 6.2 at 52 weeks. [Figure 2] [Table 4]

No major complications were seen in our study. Both case and control group not shown any case of infection. Few patients complaints of increases in pain at injection site for one or two days. Two of our cases shown swelling around heel for two to three days, which subside by conservative management. We analyzed our result statically and found that the there were statically significant difference in outcome of control and cases group. We concluded that PRP

injection at planter fasciitis site have much better outcome in relation to visual analogue score(VAS) and result difference was statistically significant.

Duration	Mean VAS Score	Std. Deviation	N
@0wk	6.593	1.0747	91
@2wk	5.26	.892	91
@4wk	3.95	.765	91
@8wk	2.82	.769	91
@12wk	1.69	.645	91
@52wk	.54	.602	91

Duration	Mean VAS Score	Std. Deviation	N
@0wk	6.466	.9936	88
@2wk	6.33	.840	88
@4wk	6.19	.800	88
@8wk	6.01	.780	88
@12wk	5.91	.866	88
@52wk	6.17	1.177	88

Figure 2- Change in VAS Score in Case and Control

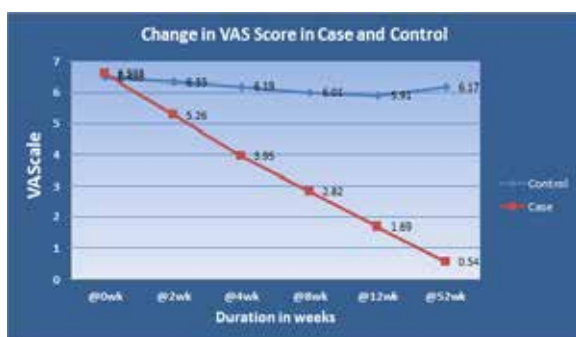


Table-4 Comparison between cases and control

Group Statistics						
Duration	Case 1	Control- 2	N	Mean VAS Score	Std. Deviation	Std. Error Mean
@0wk	1	2	91	6.593	1.0747	.1127
	2	1	88	6.466	.9936	.1059
@2wk	1	2	91	5.26	.892	.094
	2	1	88	6.33	.840	.090
@4wk	1	2	91	3.95	.765	.080
	2	1	88	6.19	.800	.085
@8wk	1	2	91	2.82	.769	.081
	2	1	88	6.01	.780	.083
@12wk	1	2	91	1.69	.645	.068
	2	1	88	5.91	.866	.092

@52wk	1	91	.54	.602	.063
	2	88	6.17	1.177	.125

Discussion

Planter fasciitis is considered to be one of the most common causes of inferior heel pain in both athletic and non-athletic population .The diagnosis is generally based on the history and the finding of localized tenderness. Many treatment option available including rest, stretching, change of footwear, low dye tapping, ultrasound therapy, laser therapy, orthotics, night splints, anti-inflammatory agent ,steroid injection and surgery in various refractory cases. Corticosteroids have a high frequency of relapse and recurrence because patient tends to bear weight after injection as a result of direct pain relief and it has been shown that it may cause planter fascia rupture, fat pad atrophy, lateral planter nerve injury secondary to injection and calcaneum osteomyelitis. Extracorporeal shock wave therapy also has recently gained popularity.

Barrett and Erredge⁴ conducted a study of chronic refractory plantar fasciitis in which 9 patients were ultrasonography- guided PRP injections in to the medial plantar fascia. At 1 year 77.9% patients reported complete resolution of symptoms.

A study was conducted by Silva and Sampio on the effectiveness of platelet rich plasma in enhancing tendon healing after an ACL reconstruction surgery.

H. Craig Fox, coal city and William Czarnecki²⁴, Chicago treated 200 patients with autologous platelet concentrate (APC). The overall success rate of patients with plantar fasciitis is was 90%. An APC revascularises tissue reduces pain and decreases edema. Follow up ultrasound after 6 months post injection almost always shows a significant reduction in the thickness of fascial bands.

Smidt et al²⁵ shown that Corticosteroids have a high frequency of relapse and recurrence. Intra tendinous injection may lead to permanent adverse changes within the structure of the tendon. Haake M et²⁶ al used Extracorporeal shock wave therapy for the management of cases of enthesopathy with variable results. A recent randomized double-blind study by M Haake et al. however, showed that this treatment is no better than placebo.²⁶ Edwards and Calandrucchio using whole blood noted a 79% success rate when treating lateral epicondylitis. The follow up time was 9.5 months, and 32% of the time, multiple injections were required.²⁰ The concentrated growth factors within PRP work in concert to initiate a healing response within a damaged tendon.

Klein et al.²⁷ have reported that transforming growth factor beta significantly increases type I collagen production in tendon sheath fibroblasts. Mishra and Pavelko²⁸ injected PRP for chronic elbow tendinosis and at a final follow up of 12-38 months, patients reported 93% reduction in pain compared with the pre injection status.

Bjrdal, et al.²⁹ performed a review of randomized placebo-controlled trials with laser therapy for tendinopathy the effect of laser therapy for patients with subacute and chronic tendinopathy. Laser therapy can reduce pain in subacute and chronic tendinopathy. Vasseljen et al.³⁰ conducted a study using a 904 nm wavelength, Ga As laser with 12 diodes covering 20 cm2. Low level laser therapy was provided at a distance of 8 mm from the skin for 10 min for a dose of 3.5 J/cm2. After dividing patients into acute and chronic cases, patients were randomized to ac-

tive laser or placebo laser. Sessions occurred 3 times/week for a total of eight treatments. Low level laser therapy was shown to have an effect over placebo; however, as a sole treatment for lateral epicondylitis, it is of limited value.

Molloy et al³¹ shown that PRP may regenerate tendon or muscle function. PRP is applied in an un-activated form that becomes activated by the collagen within connective tissue. The PRP then releases its growth factors and cytokines. These bioactive proteins in turn stimulate local stem cells and enhance extracellular matrix gene expression.

Tonk G et al.³² conducted their trial with 81 cases of chronic lateral epicondylitis and divided in to two groups. One group of 39 cases treated with local PRP infiltration and second group of 42 cases treated with low level laser therapy. They concluded that cases treated with PRP shown significant reduction in pain, increased function exceeding the effect of low level laser therapy on long term follow up

However, direct comparison with previous studies is difficult because of the different methodologies used to prepare PRP. Several systems are commercially available that allow efficient preparation for outpatient use. When selecting a preparation system, many factors must be taken into account, such as volume of autologous blood drawn, centrifuge rate/time, leukocyte concentration, delivery method, activating agent, final PRP volume and final platelet and growth-factor concentration. Due to differences in PRP characteristics, reported evidence for clinical effectiveness of PRP cannot be generalized to all of these systems. Furthermore, variation of hematologic parameters (e.g. leukocyte count, platelet count) between patients may also affect the final PRP preparation. Controversies regarding the optimal quantity of platelets and growth factors required for muscle and tendon healing still persists. Although in previous studies clinically effective PRP is defined as having at least four times the normal platelet concentration,

We in this study performed case control study to determine the effectiveness of local platelet rich plasma (PRP) infiltration in the management of planter fasciitis. We selected 179 cases and divided in to control and case group by simple randomization method. Final outcome of study was assessed by total improvement in VAS visual analogue scale in case and control group. There was marked improvement in VAScale in PRP group (case group) from mean VAS 6.6 to mean VAS 0.54 at 52 weeks. Maximum improvement in VAS score were seen during first 12 weeks of the PRP infiltration. In control group there were no improvement in VAScale and that remained from 6.5 to start with to 6.2 at 52 weeks.

Platelet-rich plasma is an autologous product produced and then used immediately at the point of care. For these reasons, it is a very safe treatment. Platelet-rich plasma will have variable efficacy based on formulation and indication, but its safety profile is very high.

Conclusion

Planter fasciitis is a very disabling disorder of foot leaving to very discomforting life and day to activity. Autologous platelet rich plasma (PRP) infiltration at the most tender part of heel is a effective method of management of these cases as compared to conservative management. This method also shown negligible complication rate and low recurrence rate. Conservative management of these cases had shown poor long term results.

Conflicts of Interest-

No potential conflict of interest relevant to this article was reported.

External Funding- None

Ethical standards

The protocol of this study was approved by the institutional review board. This study was authorized by the local ethical committee and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki as revised in 2000. The well informed written consent was obtained from every case in this study.

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