EFFICACY OF AUTOLOGOUS PLATELET RICH PLASMA IN THE TREATMENT OF PLANTAR FASCIITIS

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ABSTRACT

BACKGROUND
The study was undertaken to assess the effectiveness of autologous Platelet Rich Plasma (PRP) injection compared to local ultrasonic therapy for treatment of plantar fasciitis in terms of improvement in pain and function.

MATERIALS AND METHODS
This prospective, randomized, controlled study was conducted in Physical Medicine and Rehabilitation department of a tertiary care centre. 61 patients were randomly allocated in to either ultrasonic therapy (Group 1, n=30) or PRP group (Group 2, n=31). All patients were assessed for pain in Visual Analogue Scale (VAS) and for pain and function on Foot Ankle Disability Index (FADI) scale at baseline and three, six and twelve weeks after treatment. A p-value of less than 0.05 was considered significant.

RESULTS
Out of 61 subjects enrolled, 59 completed 12 weeks follow-up (29 in group 1, 30 in group 2). In both groups, statistically significant improvement was seen at three weeks on both VAS and FADI scales, but the observed improvement persisted upto 12 weeks follow-ups only in PRP treated group. There was no adverse event reported.

CONCLUSION
Local injection of autologous PRP proved to be a promising form of treatment. It is both safe and effective in relieving pain and improving function and superior to local ultrasonic therapy for treatment of plantar fasciitis.

KEYWORDS
Plantar Fasciitis, Heel Pain, Platelet-Rich Plasma, Ultrasonic Therapy.

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BACKGROUND

Plantar fasciitis (PF) is one of the most common causes of heel pain encountered in medical practice. Its prevalence rate is around 10% in general population.[1] It is characterised by gradual onset of sharp pain along the medial tubercle of calcaneus at the origin of plantar aponeurosis. The pain is worse with the first step taken in the morning or after prolonged sitting. Diagnosis is based on history and physical examination. Conservative management is the mainstay of treatment, and includes nonsteroidal anti-inflammatory drugs, physiotherapy, activity modification, shoe insoles, corticosteroid injection and extracorporeal shockwave therapy.[2-5]

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Ultrasound therapy is used as part of the physiotherapy regimen and is one of the most commonly employed conservative treatment for plantar fasciitis. However, the results of ultrasound therapy have been reported to be short-term and non-consistent.[6] Local steroid injection is a mode of treatment used when other conservative management yields no improvement. This too gives only a short-term relief of pain.[7] Moreover, a number of complications have been noted following local steroid injections which include plantar fascial rupture, plantar fat pad atrophy, lateral plantar nerve injury secondary to injection, and calcaneal osteomyelitis.[8-12] Thus most treatment modalities fail to give consistent results. The basis of this relative refractoriness of this condition to treatment appears to lie in the lack of inflammatory process in the pathogenesis of plantar fasciitis.[2] Researchers have demonstrated presence of degenerative changes rather than inflammatory changes in the surgical biopsy specimens of plantar fasciitis.[13-15]

Hence, a treatment regimen that initiates a healing response and regeneration rather than one that suppresses inflammatory response appears to be a rational treatment option. Platelet Rich Plasma (PRP) is one such option which

has shown promising results in a variety of clinical conditions.[15-20]

Platelet Rich Plasma is the fraction of autologous blood with significantly higher platelet count.21,22 Platelets release many bioactive proteins that are responsible for tissue regeneration and healing. In chronic conditions, PRP causes healing of chronic degenerative process due to the presence of concentrated growth factors.23

We therefore hypothesized that PRP would be an ideal treatment option in plantar fasciitis due to its capacity to promote regenerative changes. We also predicted that the beneficial effects if any would be long lasting. This study was therefore designed with an aim to assess the effect of local application of platelet rich plasma for treatment of planter fasciitis and to compare the findings with ultrasound therapy.

MATERIALS AND METHODS

The study was ethically cleared by institutional ethics committee. Informed consent was taken from each participant before inclusion in the study. Sixty-one clinically diagnosed patients with plantar fasciitis of at least 6-week duration were enrolled in the study. They were divided in two groups by closed envelop randomization. Group one patients were treated with ultrasound therapy and group 2 patients with local PRP injection. One patient from each group dropped out from the study and 59 patients completed the follow up.

Patients who had received steroid injection in inferior heel within 6 months and NSAIDS within 1 week prior to randomization and those with uncontrolled diabetes mellitus, rheumatic disease or patients with bleeding disorder were excluded from study. In patients with bilateral symptoms, the heel with more pain was included in our study. All patients were subjected to blood examination which included complete blood count with ESR, bleeding time and clotting time, serum calcium and phosphorus. Radiographs (lateral view) of the affected foot were taken to exclude any bony pathology.

All patients were assessed for subjective pain rating on visual analogue scale (VAS) and functional score using Foot Ankle Disability Index (FADI). FADI is a 26-item questionnaire that consists of 22 activity related item and 4 pain related items. Each item is scored on a 5-point scale. FADI is a percentage of 104 points in which 100% means no disability.[24]

In group 1 (n= 30), ultrasonic therapy was given on alternate days for seven sittings with frequency of 0.8 to 1.1 MHz, and intensity of 1.5 W/ cm2 at the affected heel.

Group 2 patients (n=31) received PRP injection. PRP was prepared by withdrawing 20 ml of the patient's blood in a sterile syringe containing 2.5 ml anticoagulant (CDPA). After careful mixing, blood was centrifuged at 200 Hz for ten minutes using REMI Research Centrifuge machine R- 23 ISO 9001:2000. PRP was withdrawn in a sterile syringe with a sterile lumber puncture needle from the plasma fraction, near its interface with red blood cells. A sample of the prepared PRP was sent for culture to check sterility. Platelet count of the sample was done using ammonium oxalate diluent and a count of more than 1,000,000/cmm was considered adequate. Following this, two ml. of PRP was injected locally under all aseptic conditions, using 22-gauge 1.5 inch needle. Adverse effects, (if any) were noted during each injection procedure. After injection, patients were advised ice application at injection site for two days and 500 mgs Paracetamol tablet as rescue medication for pain on need basis subject to a maximum of four tablets in a day. Routine activities were permitted from third day.

Patients were followed in outpatient department at three, six and twelve weeks, post procedure and all examinations were performed by a blinded assessor who was also a physiatrist. Primary outcome measures were Visual Analogue Scale (VAS) for pain and FADI score for functions.

In each patient the study was ended after completion of 12 weeks follow up.

Statistical Analysis

A total of 61 patients were enrolled in the study out of which 59 patients completed the follow up and were considered for analysis (30 in study group and 29 in control group).

The data was managed using Microsoft Excel and analysed using STATA (Version 9) for Windows. Chi-square test was used for comparison of binomial variables. All continuous data were expressed as mean and standard deviation of mean. Within each group, change in the mean values of continuous variables with time was compared using repeated measure analysis of variance (ANOVA) test. One way ANOVA was applied to compare mean values between the groups for each domain of continuous variables and post-hoc tests (Bonferroni correction) were used to determine significant difference between each of the groups. Results were considered significant at 5% level of significance, i.e., $p<0.05$.

RESULTS

Both the groups were comparable in respect to age and gender distribution, occupation, side involvement and baseline assessment parameters. Majority of the patients were in 25 to 45 years of age. 34 patients (57%) were homemakers.

The severity of pain at baseline as assessed by VAS score were comparable in the two groups. Ultrasound therapy group patients showed a significant improvement in VAS score at 3 weeks, but sustained improvement was not recorded at subsequent follow-ups. At six weeks, observed VAS score was significantly lower in comparison to the baseline score. However, it was not so in comparison to the score at 3 weeks. At 12 weeks, 14 patients (48.3%) reported VAS score as it was at baseline while 5 subjects (17.29%) reported increase in pain by one on VAS at 12 weeks. Mean VAS score was recorded to be 6.25±1.73 at 12 weeks, which was nearing the baseline value. It was also noted that all the patients in this group scored more than 4 on VAS at 12 weeks.

Ultrasound therapy group showed similar findings on FADI score. A statistically significant improvement ($p<0.001$) was found at 3 weeks that was sustained at 6 weeks of follow-up but deteriorated to about baseline level at 12 weeks. Both the activity and pain components of FADI showed same trend throughout the study period.

PRP group showed consistent improvement till the end of the study period. Significant improvement in pain was observed in this group as revealed by reduction in VAS score at all three follow-ups ($p<0.001$). When compared with baseline VAS score at 3 weeks, 6 weeks and 12 weeks were found to be significantly lower. Significant difference was also observed between the VAS scores at 3 weeks and 6 weeks as well as 6 weeks and 12 weeks. Twenty-one patients (70%) reported mild pain (VAS ≤ 2) and 6 patients (20%) no pain (VAS-0) at 12 weeks of follow-up. No patient in this group had VAS more than 3 at 12 weeks.

Similarly, FADI score was also found to be improved after PRP injection. Highly significant improvement ($p< 0.0001$) in FADI score was recorded at 3, 6 and 12 weeks when compared with baseline score. The maximum improvement of FADI scores was observed at first follow-up (3 weeks). However, the improvement was also significant from 3 weeks to 6 weeks and 6 weeks to 12 weeks.

Group	At Baseline	At Three Weeks	At Six Weeks	At Twelve Week
UST * (n-29) (Group- 1) Significance of Change over Baseline	6.50 ± 1.62	5.57 ± 1.81 P <0.0001	5.57 ± 1.95 Non-significant	6.25 ± 1.73 Non-significant
PRP † (n-30) (Group- 2) Significance of Change over Baseline	7.40 ± 1.10	4.30 ± 1.51 P <0.0001	2.67 ± 1.24 P <0.0001	1.30 ± 0.91 P <0.0001

Table 1. Visual Analogue Scale Score. * Ultrasound Therapy, † Platelet Rich Plasma

Group	At Baseline	At Three Weeks	At Six Weeks	At Twelve Weeks
UST * (n-29) (Group- 1) Significance of Change over Baseline	54.01 ± 11.41	59.59 ± 12.33 P <0.0001	60.53 ± 12.16 Non-significant	55.72 ± 11.28 Non-significant
PRP † (n-30) (Group- 2) Significance of Change over Baseline	53.88 ± 9.74	68.32 ± 11.64 P <0.0001	81.82 ± 9.26 P <0.0001	90.05 ± 5.42 P <0.0001

Table 2. Foot Ankle Disability Index Score (Total). * Ultrasound Therapy, † Platelet Rich Plasma

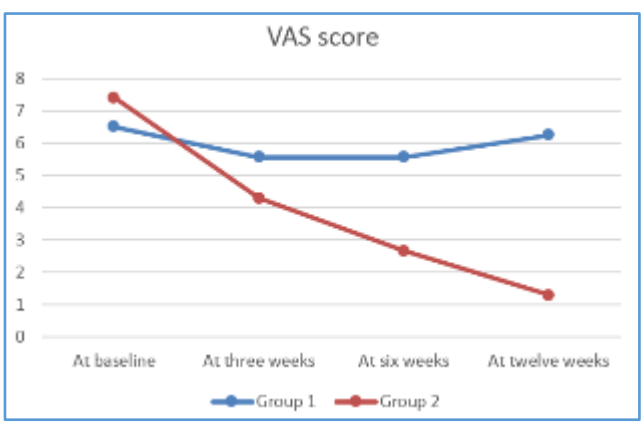

Figure 1. Changes in VAS score following Treatment

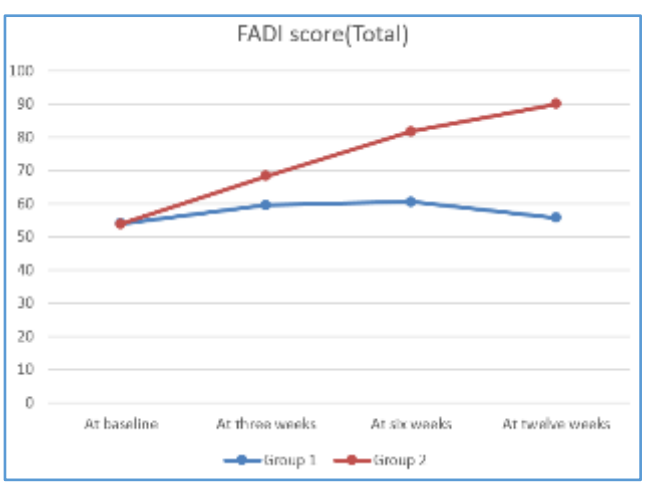

Figure 2. Changes in Foot Ankle Disability Index Score (Total) following Treatment

DISCUSSION

Plantar fasciitis is an overuse injury of the heel involving repeated micro-tears at the site where the plantar fascia inserts into the calcaneus. Symptoms most often occur during the first few steps in the morning but may also occur during intense activity or after prolonged standing. Risk factors such as low or high arches, over-pronation of the foot, systemic disease, and obesity have been reported. Histologically plantar fasciitis is not an inflammatory condition, but a chronic degenerative one, characterized by infiltration with macrophages, lymphocytes, and plasma cells, tissue destruction and repair involving immature vascularisation and fibrosis. The normal fascia tissue is replaced by an angiofibroblastic hyperplasic tissue which spreads itself throughout the surrounding tissue creating a self-perpetuating cycle of degeneration.[2] Hence, plantar fasciitis is relatively resistant to conventional treatment modalities especially those with anti-inflammatory effects. This observation forms the basis of using PRP for its treatment. Growth factors released from α granules of platelets are known to play a central role in the healing process and tissue regeneration. Platelets release platelet derived growth factor (PDGF), transforming growth factor β, insulin like growth factor 1(IGF1), vascular endothelial growth factors etc that have a beneficial effect in tissue repair and regeneration[25] and therefore may provide beneficial effect in plantar fasciitis.

Plantar fasciitis, has been reported in people from 7 to 85 years but is usually observed in the 40-60 year age group. It is more common in females[26] and in people with

occupations that necessitates continual standing or walking, such as waiters, maids, and kitchen workers.[27] Our study also showed female predominance and most of our patients were home makers. These findings are consistent with earlier studies.[26,27]

Our results in PRP group are comparable with Omar et al who found reduction in mean VAS score from 8.2±1.3 at baseline to 2.6±2.1 at 6 week ($p < 0.001$). They also found highly significant improvement in Foot Health Status Questionnaire (FHSQ) ($p < 0.001$). They concluded that local injection of autologous PRP is a promising form of therapy for plantar fasciitis. It is both safe and effective in relieving pain and improving function in plantar fasciitis.28

Barret et al enrolled 9 patients in a pilot study to evaluate PRP injection with plantar fasciitis.29 All patients demonstrated hypo-echoic and thickened plantar fascia in ultrasound. They injected 3 ml. of autologous PRP under ultrasound guidance. They documented reduction in thickness of plantar fascia as well as change in signal intensity. Clinically six out of 9 patients were found to achieve complete resolution of symptoms after 2 months. At 1 year 77.9% patients had complete resolution of symptoms. In another study, Baz et al also recorded similar findings and recommended ultrasound guided PRP injection for chronic plantar fascitis.[30] Comparable clinical improvement was also observed in our study, although our injection procedure was not done under ultrasound guidance.

Patients in our UST group showed improvement at 3 weeks but this observation did not last for further follow-ups. In fact, some patients of this group even reported increase in VAS score. These results are comparable with those of Crawford et al. who observed no statistically significant ($p < 0.5$) improvement in therapeutic ultrasound treated group.[31]

The current study revealed that local injection of autologous PRP is a promising form of treatment for plantar fasciitis as PRP treated group showed greater degree of improvement compared to UST treated group, reflecting better efficacy. No side effects were noted following the procedure. Hence, it is both safe and effective in relieving pain and improving function.

CONCLUSION

Local injection of PRP is a novel form of treatment and the study highlights growing importance of PRP in chronic degenerative musculoskeletal conditions. The local PRP injection is well tolerated with no major complications. However, sustained efficacy of this promising and safer therapeutic option should be further evaluated in longitudinal follow-up studies with larger number of patients.

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