The efficacy of platelet rich plasma in the treatment of resistant plantar Fasciitis-follow up of 12 months

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Abstract

Background: Platelet-rich plasma (PRP) has been used as an alternative therapy for plantar fasciitis (PF) to reduce heel pain and improve functional restoration. PRP has a role in the inflammatory, coagulation processes as well as immunity modulation. During the degranulation of platelets they release cytokines and other growth factors. These promote angiogenesis, help in tissue remodelling and wound healing. They may have a pain relieving effect depending on the release of proteases with analgesic properties. This is a study of 26 patients treated with PRP for the treatment of resistant PF.

Objective: To compare the efficacy of local injection of PRP at different time intervals for the treatment of resistant PF

Materials and methods: In this study, 26 patients diagnosed with resistant Plantar Fasciitis, underwent local injection of PRP and were followed up at 3, 6, 9 and 12 months and VAS recorded.

Results: In this study, the VAS showed significant improvement from the pre injection VAS to the VAS at 3 months, 6 months, 9 months and 12 months after injection. The difference in the VAS from 3 months to 6, 9 and 12 months post was statistically significant. The difference in VAS from 6 months to 9 months and 12 months post injection was statistically highly significant and very highly significant respectively. In between 9 months to 12 months post injection, there was no statistical significance.

Conclusion: Platelet Rich Plasma provides good symptomatic relief in the treatment of Plantar Fasciitis with sustained gradual relief of pain and improving daily function and activity level. Platelet Rich Plasma proved to be effective modality in providing continuous and sustained relief of pain over a period of 12 months.

Keywords: Platelet rich plasma, Fasciitis-follow

Introduction

Plantar Fasciitis (PF) presents with severe pain in the heel after a period of rest or with the first few steps of the day which alleviates with movement of the foot [1]. The exact etiology of PF is not known but it is postulated that it is mainly caused due to overloading of the plantar foot muscles. The risk factors for the development of PF include; obesity, flat feet, limb length discrepancy and overuse. Tightness of the Achilles tendon and inappropriate foot wear has also been proven to cause plantar fasciitis [2].

The various modalities for the treatment of PF include activity and lifestyle modifications, night splints, orthotics and special foot wears, extracorporeal shockwave therapy and casting. Corticosteroid injection and Platelet Rich Plasma (PRP) injection over the medial tuberosity of the Calcaneum is an effective treatment modality once conservative management doesn’t provide relief to the patient. Of late PRP, which is bioactive with a platelet concentration 2-5 times the baseline platelet count of the patient is been used in the treatment [2].

PRP has a role in the inflammatory, coagulation processes as well as immunity modulation. During the degranulation of platelets they release cytokines and other growth factors. These promote angiogenesis, help in tissue remodelling and wound healing. They may have a pain relieving effect depending on the release of proteases with analgesic properties.

Research is being done on PRP and its beneficial effects in chronic tendinopathies as well as treatment in cosmetic, dental and wound healing therapies.

Materials and Methods

This is cohort of 26 patients with resistant PF treated with PRP. The inclusion criteria includes
all Patients with chronic heel pain and with confirmed diagnosis of Idiopathic PF from 30 to 60 years of age and exclusion criteria include Patients with Diabetes Mellitus, Rheumatoid Arthritis, Gout, Patients with history of trauma to foot or congenital foot deformity, Patients who have had previous foot surgery, BMI > 40, Anaemia (Hb<7)and Pregnant women. Patient demographics were recorded. Through history taken and complete clinical examination of foot performed and lateral and antero-posterior x-rays of the foot were done to confirm the diagnosis and rule out other causes of heel pain. In bilateral cases, only the more painful side was recruited into our study.

Patients were asked to report the pain they experience using the Visual Analogue Score (VAS) and were recorded on the scale of 0-10 where 0 was pain free and 10 was pain imaginable.

Injections were given on the basis of direct palpation of the most tender area by using the Pitting technique (20 times).

PRP Preparation Technique
A 20 ml sample of venous blood was drawn from the patient’s Cubital vein and transferred equally into 4 Vacutainers containing buffered sodium citrate (BD Vacutainer, manufactured at Becton, Dickinson and Company, 1 Becton Drive, Franklin Lakes, NJ, USA).

The sample were then placed in a centrifugation machine (REMI R-8CBL, REMI ELEKTROTECHNIK LTD, VASAI INDIA) and centrifuged at 2400rpm for 10 minutes. Using a 18G spinal needle (BD Spinal Needle) the buffy coat and supernatant platelet poor plasma layer was aspirated, and transferred to 2 plain vacutainers in equal volumes.

The collected sample were again centrifuged at 3600rpm for another 15 minutes. The supernatant platelet poor plasma was then aspirated using a 10 ml syringe and an 18G spinal needle and discarded. The sediment PRP was aspirated and was then transported to the Procedure room of the Orthopaedic outpatient department under aseptic precautions.

3 ml PRP was aspirated from the syringe that was transported to the OPD using a 18G needle and 5cc syringe and injected into the medial calcaneal tubercle at the point of maximum tenderness under aseptic precautions.
After injection, all the patients were prescribed analgesics (Aceclofenac 100mg + Paracetamol 325mg) twice daily for one week with local heat fomentation and analgesic gel after 48 hours post injection and were advised restriction of moderate to severe activities for a period of 2 weeks. All the patients were followed up at 3 and 6 months but at 9 months, 1 patient did not report for follow up at 9 months and at 12 months respectively. The dropout rate being 3.85% at 9 months and 3.85% at 12 months. All the patients were interviewed over telephone and VAS was recorded for the particular follow-up interval. Statistical analysis was carried out using SPSS version 17.0. Students unpaired t test, Chi-square test, ANOVA - Fisher's F test and Bonferonni t test were carried out. 

\( p < 0.05 \) was considered to be significant.

### Results

In our study, 26 patients with idiopathic PF received PRP injection. We compared the efficacy of PRP using the VAS at 3 months, 6 months, 9 months and 12 months post injection.

### Table 1: Patient Demographics

|                | Mean | SD  |
|----------------|------|-----|
| Age (years)    | 43.15| 9.649 |
| Gender         |      |     |
| Male           | 10   | 38.5% |
| Female         | 16   | 61.5% |
| Side           |      |     |
| Right          | 19   | 73.1% |
| Left           | 7    | 26.9% |
| Duration of pain (months) | 6.42  | 5.818 |
| BMI            | 27.54| 3.373 |

### Table 2: Comparison of VAS at different intervals

| Duration       | Pre Injection VAS | 3 months VAS | 6 months VAS | 9 months VAS | 12 months VAS | F     | P          |
|----------------|-------------------|--------------|--------------|--------------|---------------|-------|------------|
| t              | 1.601             | 6.036        | 0.567        | 7.113        | 11.91         | 131.72| <0.001 vhs |
| p              | 0.116 ns          | <0.001 vhs   | 0.573 ns     | <0.001 vhs   | <0.001 vhs    |       |

### Table 3: Multiple Comparisons at different intervals (Bon Fer semi t test)

| group | (I) VAS at time | (J) VAS at time | Mean Difference (I-J) | P       |
|-------|----------------|----------------|-----------------------|---------|
| PRP   | Pre injection  |                |                       |         |
|       | 3 months       | 3.077          | <0.001 vhs            |         |
|       | 6 months       | 5.022          | <0.001 vhs            |         |
|       | 9 months       | 6.346          | <0.001 vhs            |         |
|       | 12 months      | 6.982          | <0.001 vhs            |         |
|       | 3 months       | 1.945          | <0.001 vhs            |         |
|       | 9 months       | 3.269          | <0.001 vhs            |         |
|       | 12 months      | 3.905          | <0.001 vhs            |         |
|       | 6 months       | 1.325          | 0.002 hs              |         |
|       | 9 months       | 1.960          | <0.001 vhs            |         |
|       | 12 months      | 0.635          | 0.716 ns              |         |

Vhs: very highly significant hs: highly significant ns: non significant

The VAS in this study showed significant improvement from the pre-injection VAS to the VAS at 3 months, 6 months, 9 months and 12 months after injection with \( p \) values <0.001. The difference in the VAS from 3 months to 6, 9 and 12 months post was statistically significant \( (p = <0.001) \). The difference in VAS from 6 months to 9 months and 12 months post injection was statistically highly significant and very highly significant respectively \( (p = <0.002 \) and \( p = < 0.001) \). In between 9 months to 12 months post injection, there was no statistical significance with mean difference of VAS being 0.635 with \( p \) values being 0.716. This shows that maximum benefit of PRP injection was there till 9 months. If the patient is not symptomatically better this can be considered as an indication for another injection of PRP at 9 months.

### Discussion

This study was designed to compare the efficacy of local injection of PRP at different time intervals for the treatment of resistant PF. PRP contains a more concentrated amount of platelets than does whole blood. Within the platelets, there are...
powerful growth factors, including platelet-derived growth factor, transforming growth factor beta and epidermal growth factor. The injection of PRP into the affected tissue initiates the healing stages necessary to reverse the degenerative process at the base of the plantar fascia. The individual cytokines present in the platelet alpha granules have been shown to enhance fibroblast migration and proliferation, up-regulate vascularisation and increase collagen deposition in a variety of in vitro and in vivo settings [3]. Additionally, many of these cytokines have been seen to work in a dose dependent manner. The concentrated growth factors work in a synergistic manner to initiate a tendon healing response. Transforming growth factor beta 1 is shown to significantly increase type I collagen production by tendon sheath fibroblasts. This same mechanism is likely to be active in chronic PF.

The age range of the patients in our study being 30 years to 60 years with mean age of 43.15 years. There were 10 male patients (38.5%) and 16 female patients (61.5%). BMI of the patients in our study with 5 patients in the BMI less than 25 group and 21 patients in the BMI greater than or equal to 25 group with a mean BMI of 27.54.\[4\]. The mean Pre injection VAS of the patients in our study was 7.46. The duration of pain (symptom) of the patients in our study ranging from 2 months to 2 years with mean duration of 5.818 months.

In this study, we found that there was a significant decrease in the pain as time progressed from the first visit to their last visit at 12 months. This was observed by the decreasing VAS which was statistically significant (\(p<0.001\)). At 3 months post injection, the mean VAS was 4.38. At 6 months post injection, the VAS being 2.44 and at 9 and 12 months, the VAS being 1.12 and 0.48 respectively. The difference in the VAS from 3 months to 6, 9 and 12 months post injection was statistically significant (\(p = <0.001\)). The difference in VAS from 6 months to 9 months and 12 months post injection was statistically highly significant and very highly significant respectively (\(p = <0.002\) and \(p = < 0.001\)). In between 9 months to 12 months post injection, there was no statistical significance with mean difference of VAS being 0.635 with \(p\) values being 0.716.

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Rahim A, Tiwari M in a comparative study from June 2013 to December 2014 evaluated the outcomes of PF treated with PRP against steroid injections. 163 patients received PRP injections and 158 patients received steroid injections into the plantar fascia and were assessed using the VAS at 4, 8, 12, 26 and 52 weeks after the procedure. Their results were similar to the results of our study with regard to progressive pain relief with single PRP injection over a period of 1 year [4].

Martinelli N et al. in 2008-2009 studied the use of PRP in chronic PF in 14 consecutive patients. They were injected with PRP and subjective scores taken, they were followed up after 12 months. 11 patients had a decrease in the VAS. There was significant decrease in VAS from 7.1 \(\pm\) 1.1 before treatment to 1.9 \(\pm\) 1.5 at the last follow-up (\(p<0.01\)). This further substantiates the fact that PRP was a safe alternative and had a potential to decrease the pain due to this condition [5].

Ragab EM et al. between February 2010 and June 2011, studied on 25 patients with PF who underwent treatment with PRP injections. They noted that 22 patients showed subjective improvement and 15 patients had better functional outcome. The average pre-injection VAS was 9.1 (range 8–10). Post-injection, using the same VAS scale the pain decreased to average of 1.6 (range 0–6) (\(p<0.001\)). USG showed significant changes in the thickness of the plantar fascia as well as signal intensity in the region of injection of the PRP [6].

Peerbooms et al. in their study concluded that the concentrated growth factors work in a synergistic manner to initiate a tendon healing response. This hypothesis is supported by in vitro research in the literature. Transforming growth factor \(\beta 1\) is shown to significantly increase type I collagen production by tendon sheath fibroblasts. This same mechanism is likely to be active in chronic plantar fasciitis [7].

Wilson et al. in their prospective case series on patient reported pain and disability following PRP injection in patients with chronic plantar fasciitis. They concluded that PRP is a safe therapeutic option with the ability to decrease heel pain in patients with chronic plantar fascitis not responding to conservative management [8].

Previous studies described PRP injection as an effective treatment option for chronic PF. PRP is beneficial in its own way, with fewer complications, but the need for a centrifuge machine that is expensive and is the mainstay for anyone who wants to give PRP in an outpatient facility and thus increases the cost of it by at least 6-8 times more than that of corticosteroids.

The limitations of our study being less number of patients. When compared to the study done by Mahindra P, Yamin M, Sehi H.S et al. [9] in 2016, the lack of objective and quantifying diagnostic tool such as a USG-scan or an MRI to confirm the diagnosis and changes in the plantar fascia thickness after injection which allows better insight and therefore a quantification of the efficacy of injection and also the post-injection changes in the fascia. The absence of ultrasound guidance for accurate needle placement and delivery of PRP injections was also a limitation of our study. We accept that this may arguably allow for more accurate placement of the injection, and could be considered, but a randomized control trial done by Tsai et al. [10] showed no advantage of ultrasound guidance over direct palpation of the most tender area, when steroid was injected for PF.

Conclusion

In this study, we conclude that Platelet Rich Plasma provides good symptomatic relief in the treatment of Plantar Fasciitis with sustained gradual relief of pain and improving daily function and activity level. Platelet Rich Plasma proved to be effective modality in providing continuous and sustained relief of pain over a period of 12 months. The maximum benefit of PRP injection was there till 9 months and hence can be considered as an indication for another PRP injection. There were no complications related to the technique of injection.

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