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Abstract

Background: Chronic plantar fasciitis is a common orthopedic condition that can prove difficult to successfully treat. In this study, autologous platelet-rich plasma (PRP), a concentrated bioactive blood component rich in cytokines and growth factors, was compared to traditional cortisone injection in the treatment of chronic cases of plantar fasciitis resistant to traditional nonoperative management.

Methods: Forty patients (23 females and 17 males) with unilateral chronic plantar fasciitis that did not respond to a minimum of 4 months of standardized traditional nonoperative treatment modalities were prospectively randomized and treated with either a single ultrasound guided injection of 3 cc PRP or 40 mg DepoMedrol cortisone. American Orthopedic Foot and Ankle Society (AOFAS) hindfoot scoring was completed for all patients immediately prior to PRP or cortisone injection (pretreatment = time 0) and at 3, 6, 12, and 24 months following injection treatment. Baseline pretreatment radiographs and MRI studies were obtained in all cases to confirm the diagnosis of plantar fasciitis.

Results: The cortisone group had a pretreatment average AOFAS score of 52, which initially improved to 81 at 3 months posttreatment but decreased to 74 at 6 months, then dropped to near baseline levels of 58 at 12 months, and continued to decline to a final score of 56 at 24 months. In contrast, the PRP group started with an average pretreatment AOFAS score of 37, which increased to 95 at 3 months, remained elevated at 94 at 6 and 12 months, and had a final score of 92 at 24 months.

Conclusions: PRP was more effective and durable than cortisone injection for the treatment of chronic recalcitrant cases of plantar fasciitis.

Level of Evidence: Level I, prospective randomized comparative series.

Keywords: platelet-rich plasma, PRP, cortisone injection, plantar fasciitis, heel pain

Chronic plantar fasciitis is a common orthopedic problem that affects 10% of the population.^{44,45,50} It can be difficult to treat in severe cases and represents an extensive annual economic burden with direct costs to third party payers in the United States estimated at up to \$376 million in 2007.⁵⁶ The pathophysiology remains poorly understood, but appears similar to Achilles tendinopathy with microscopic degenerative injury and local disruption of the collagen matrix and microtears rather than a failed healing response.⁵ The presence of erratic blood flow with zones of hypovascularization and hypervascularization also plays a role in the disease process.^{25,29} Clinical findings of chronic plantar fasciitis include local tenderness and associated stiffness due to soft tissue tightness and contracture with common patient complaints of morning pain and heel discomfort with initiation of ambulation.⁵⁷

A myriad of nonoperative and operative approaches have been utilized without uniform or reproducible success. Nonoperative approaches include rest, heel cups,

stretching, orthotics, immobilization, nonsteroidal and steroidal anti-inflammatory medication, and physical therapy.⁵⁷ Cortisone usage, autologous blood injection, and extracorporeal shock wave therapy have also been used with variable success.^{1,6,13,27,30,58} Because traditional nonoperative management of chronic plantar fasciitis still fails in 10% to 15% of patients, numerous surgical treatments have been explored including, open, endoscopic and percutaneous fascial release with varying clinical outcomes.^{8,24,57} Concerns regarding increased stresses on the ligaments and bones of the midfoot and forefoot resulting from surgical release of the plantar fascia persist. MRI and

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ultrasound techniques have proven useful in assessing the response of plantar fascial injuries to various operative and nonoperative approaches in an objective, quantifiable, comparable, and reproducible manner.^{41,46,57}

Recently, platelet-rich plasma (PRP) has been proposed as a potential treatment for chronic plantar fasciitis. PRP is a bioactive component of whole blood with concentrations of platelets above baseline values.^{9,22,32,60} Platelets play a critical role in the normal injury repair cycle of the body as well as modulating intercellular communication.^{3,9,22} The platelets secrete a wide variety of cytokines and growth factors that act as chemo-attractants for reparative cells.^{2,3,9,14} These agents include platelet-derived growth factor (PDGF), transforming growth factor-beta 1 (TGF- β 1), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), hepatocyte growth factor (HGF), and connective tissue growth factor (CTGF). These growth factors modulate neovascularization and angiogenesis, promote mitogenesis, boost local collagen production, and provide anti-inflammatory effects by blocking cyclooxygenase-2 (COX-2) enzyme production.^{2,3,7,9,14,15,18,34,36,53}

The different cellular sizes and densities among platelets, red blood cells, and white blood cells allow their isolation through centrifugation.²² By mechanically concentrating the level of platelets to levels 7 to 10 times baseline by simple centrifugation of whole blood, correspondingly high levels of these growth factors are obtained.^{14,22,34,37} Levels of PDGF in PRP can range have been measured as high as 25 \times baseline value, while EGF, TGF- β , and VEGF levels can rise to 10 \times baseline depending on the system used.^{2,14,17,22} These findings have led to the use of PRP as a vector to deliver growth factors to local muscle and tendon injury and repair zones to induce and accelerate healing.^{2,3,9,14,18,19,23,36,38,51-53,55,59} PRP was first used in dental, maxillofacial, and plastic surgery in the early 1990s and more recently to promote anastomotic healing in coronary bypass surgery.^{22,32} Recently, PRP has shown promise in the treatment of various musculoskeletal conditions including chronic lateral epicondylitis, osteoarthritis, muscle strain, ligament sprain, cartilage damage, fractures, and tendon injury and has been approved by the International Olympic Committee in the treatment of soft tissue injuries and tendon disorders.^{2,4,10-12,14-16,20,21,26,37,39,40,42,43,47-49,54}

Methods

Forty patients with chronic unilateral plantar fasciitis who had failed extensive traditional nonoperative management were randomized into 2 groups for prospective treatment and evaluation. Group 1 was treated with a single ultrasound guided (General Electric LOGIC Book XP) injection

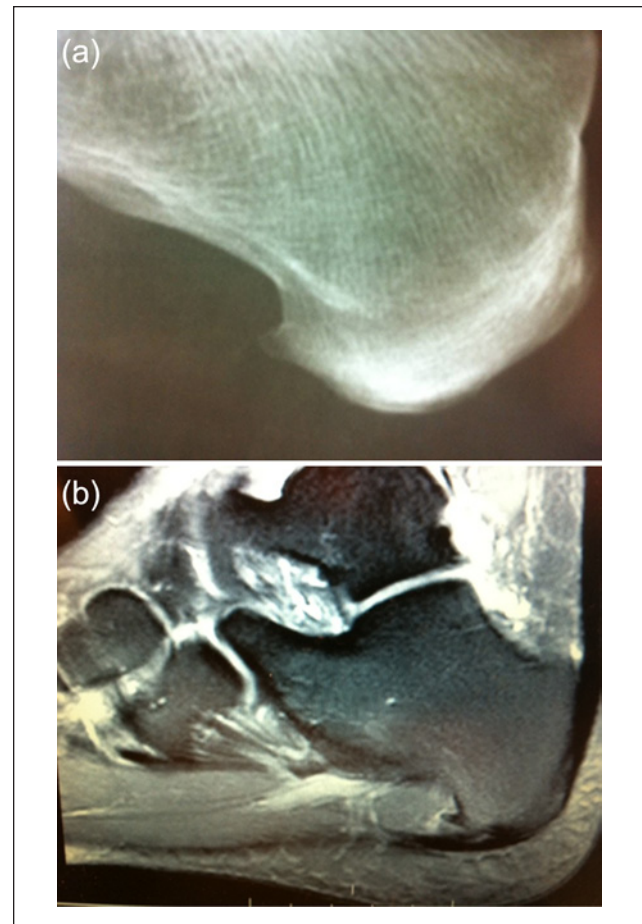


Figure 1. (a) Plain radiograph of calcaneus with typical adaptive spur formation. (b) T2-weighted MRI image demonstrating typical findings of plantar fasciitis with plantar fascial thickening, tearing, spur formation, and reactive bone edema.

of 40 mg DepoMedrol cortisone (Pharmacia & Upjohn Co, New York, NY), and group 2 was treated with a single ultrasound guided injection of autologous PRP. For the purposes of this study, chronic refractory plantar fasciitis was defined as those patients who had experienced at least 4 months of heel pain despite a standardized trial of traditional nonoperative treatment including rest, physical therapy (minimum 6 weeks), silicone heel lifts (minimum 4 weeks), CAM walker bracing or cast immobilization (minimum 4 weeks), night splinting (minimum 4 weeks), and nonsteroidal medication. All patients were screened with plain radiographs and MRI to confirm the diagnosis of plantar fasciitis (Figures 1a and 1b).

All patients gave informed consent and the study was approved by an institutional review board. The PRP preparation system used in this study was the Accelerate Sport Platelet Concentration System (Exactech, Inc, Gainesville, FL). In this study a 27 cc venous blood sample was obtained from the patient and mixed with 3 cc of anticoagulant citrate

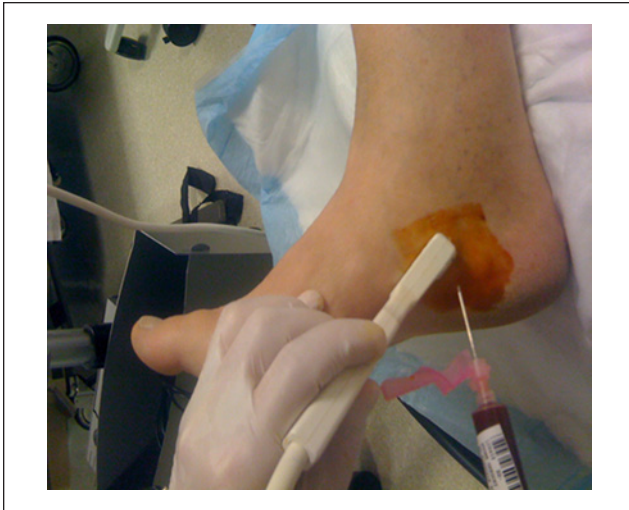


Figure 2. Single-entry-point ultrasound-guided needle placement technique.

dextrose solution formula A (ACD-A) to prevent clotting of the sample. This sample was then centrifuged at 2400 rpm for 12 minutes using a soft spin (zero braking) technique to minimize mechanical damage to the platelets. A 3 cc PRP unbuffered and unactivated isolate was then obtained from the “buffy coat” of the centrifuged blood sample. With the patient lying in a supine (Figure 2) position, the injury zone was prepped in both groups using 2% chlorhexadine gluconate/70% isopropyl alcohol and then a local anesthetic field block was performed by the same individual in all cases using a 23 gauge needle with a total of 6 cc of 0.5% Marcaine (bupivacaine; Hospira, Lake Forest, IL). The block was placed medially with 2 cc of 0.5% Marcaine injected into the skin, 2 cc into the fascial tissue, and 2 cc into the periosteum of the medial calcaneal tubercle. Following injection with either PRP or DepoMedrol into the injury site, patients were placed into a cam walker brace for 2 weeks and allowed to return to activities as tolerated along with a daily home eccentric exercise (Swedish heel drop program) and calf/arch stretching regimen. Nonsteroidal anti-inflammatory use was not permitted during the first 2 weeks after treatment and was discouraged throughout the entire study period. No other treatment modalities were used during the study. Interval AOFAS hindfoot scoring data and physical examinations were completed by an investigator blinded to the treatment modality immediately prior to injection, then repeated at 3, 6, 12, and 24 months after treatment.

Statistical Analysis

All data analysis was completed using a pre-established plan with categorical values being compared using a Pearson chi-square test. Pretreatment continuous variables

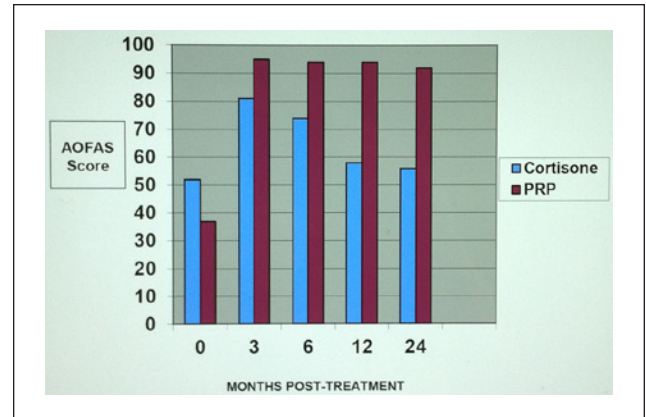


Figure 3. Graph demonstrating the clinical superiority of PRP versus cortisone for severe chronic Achilles tendinosis over a 2-year period ($P = .001$, 95% CI).

were compared using the Student *t* test. The AOFAS scores were compared with an analysis of variance with the repeated measurements test. The level of clinical significance was set at $P = .05$ with a confidence interval of 95% for all tests.

Results

The cortisone group included 9 males and 11 females with an average age of 59 (range, 24 to 74) years. Symptoms averaged 5.4 (range, 4 to 24) months in duration prior to treatment. The cortisone group had a pretreatment average AOFAS score of 52 (range, 24 to 60), which initially improved to 81 (range, 56 to 90) at 3 months posttreatment, but decreased to 74 (range, 54 to 87) at 6 months, returned to near baseline levels of 58 (range, 45 to 77) at 12 months posttreatment, and had a final 24 posttreatment score of 56 (range, 30 to 75). The PRP group had 8 males and 12 females with an average age of 51 (range, 21 to 67) years. They averaged 5.7 (range, 4 to 26) months of symptoms prior to treatment.

In contrast to the cortisone group results, the PRP group started with an average pretreatment AOFAS score of 37 (range, 30 to 56), which increased to 95 (range, 88 to 100) at 3 months, remained elevated at 94 (range, 87 to 100) at 6 months, was 94 at 12 months (range, 86 to 100), and had a final 24-month posttreatment score of 92 (range, 77 to 100) (Figure 3). The difference between the posttreatment AOFAS scoring results of the cortisone and PRP groups was clinically significant ($P = .001$, 95% CI) at 3-, 6-, 12-, and 24-month follow-up evaluations. The duration of symptoms prior to injection treatment did not have any clinically significant impact on the results in either group.

Although some variance was seen among height, weight, and body mass index (BMI) among the groups, the differences did not reach statistical significance. The male

patients in the PRP group averaged 182.6 cm in height (range, 175.3-190.5) and 98.6 kg in weight (range, 77.1-127.0) and had an average BMI of 29.5 kg/m³ (range, 25.1-36.9). The male patients in the cortisone group averaged 182.9 cm in height (range, 157.5-200.6) and 89.9 kg in weight (range, 73.0-115.7) and had an average BMI of 27.87 kg/m³ (range 23.0-29.9). The female patients in the PRP group averaged 170.5 cm in height (range, 152.4-195.6) and 70.8 kg in weight (range, 72.6-108.9) and had an average BMI of 29.2 kg/m³ (range, 25.1-34.0). The female patients in the cortisone group averaged 165.5 cm in height (range, 160.0-170.2) and 70.4 kg in weight (range, 68.0-95.3) and had an average BMI of 30.6 kg/m³ (range 23.5-35.0).

Discussion

The successful use of PRP formulations to treat chronic tendinopathies led to its application in treating severe cases of plantar fasciitis.^{1,28,31,41} Lopez-Gavito et al surveyed a small group of patients with a minimum of 12 months of severe chronic plantar fasciitis and/or Achilles tendinosis and noted AOFAS hindfoot score improvement from 39 to 97 by a month and average Visual Analogue Scale (VAS) pain scores dropping from 9 to 2 after PRP treatment.²⁸ No control group was provided in this investigation. In another small, nonblinded preliminary study without a control group, Martinelli et al used 3 weekly injections for chronic plantar fasciitis and noted average VAS scores decreased from 7.1 to 2.1 after 12 months with excellent final results in 9 patients, good results in 4, and poor in 1.³¹

Ragab and Othman followed a group of 25 patients with chronic plantar fasciitis treated with PRP without a control group for an average of 10.3 months and documented VAS score improvement from 9.1 to 1.6.⁴¹ Prior to treatment 72% of their patients noted severe activity limitations, while 28% were moderately limited, but after PRP treatment 92% had little or no noticeable limitations. Ultrasonography demonstrated decreased plantar fascial thickening after PRP treatment but no control group was provided in that study.

In the only controlled study other than ours comparing PRP and cortisone treatment of chronic plantar fasciitis, Akashin et al prospectively examined 60 patients who had failed 3 months of conservative care.¹ The patients were treated in 2 nonrandomized consecutive groups of 30 with either 40 mg methylprednisolone or 3 cc of PRP and then followed for 6 months posttreatment. Mean VAS scores improved from 6.2 to 3.2 in the steroid group and 7.33 to 3.93 in the PRP group after 6 months.

In our single-blinded, prospective, randomized, longitudinal case series, the use of local PRP injection proved more successfully than cortisone injection in the long-term management of severe chronic plantar fasciitis in

cases where prolonged traditional nonoperative treatment had failed. The likely mechanism of this effect is the release of growth factors and chemoattractants from the highly concentrated platelets in the plantar fascial injury zone.^{6,9,22,37,38,59} These platelet nests may act as rally points for the local recruitment of macrophages and fibroblasts to gradually repair the damaged collagen of the tendon following platelet activation. This can lead to modulation of angiogenesis and local blood flow to assist correction of a failed healing response.^{15,25} Collagen processing is improved with the in-migration of fibroblasts.^{17,39} The finding that the majority of improvement seen in our patients occurred in the first month following the PRP injection suggests an early anti-inflammatory effect possibly due to the inhibition of cyclo-oxygenase-2 (COX-2) enzymes by the cytokines in PRP.^{22,53} The long-term excellent durability of clinical success in the PRP group in this 2-year study may be the result of improved collagen upregulation and neovascularization.

In contrast to the encouraging results demonstrated in the PRP group in this study, the cortisone group long-term results were disappointing. Although initial results at 3 months postinjection were encouraging, subsequent clinical scoring at 6, 12, and 24 months quickly degraded. With the number of subjects available in this study, no significant difference was noted between the pretreatment and posttreatment results in the cortisone group after 12 and 24 months.

The strengths of this study are its randomized and prospective longitudinal nature, the long length of follow-up, and its high subject retention rate. The single-blinded nature of the study is not as optimal as a double blinded study, however, and this is the primary flaw of the study.

Since similar injection techniques were used in both groups, it is unlikely that the long-term clinical success of PRP treatment over cortisone in this study was due to any mechanical effects as described in dry needling or brisement procedures.²² There was difference in the volume of injection between the study groups with 9 cc in the PRP group (3 cc PRP + 6 cc block) and 7 cc in the DepoMedrol group (1 cc DepoMedrol + 6 cc block), but the impact of this on the study results is uncertain.

The accelerated healing and recovery seen in the use of PRP in plantar fasciitis has also been seen in studies focusing on utilizing PRP to augment Achilles reconstruction for full thickness tears.^{4,18,48} The enhancing effects of PRP injection have also been demonstrated when used for chronic tennis elbow and patellar tendonitis management and following acute muscle injury.^{9,22,23,26,36-38,52,53,55} Early encouraging results have also been reported in the use of PRP augmentation for rotator cuff reconstruction, flexor tendon, and anterior cruciate ligament repair.^{2,16,17,19,21,25,29,39,40,42,43,54,59} Future research will focus on optimization of the growth factor concentration in PRP, the effects of white blood cells, and the systemic results of PRP treatment.^{33,35,60,61}

Despite the long-term success of PRP in treating these cases of chronic severe plantar fasciitis, the fundamental treatment paradigm of rest, ice, eccentric exercise, activity modification, and selective immobilization is still successful in the majority of patients with mild to moderate disease and should not be abandoned. The PRP system used in this study added approximately \$300 per case. Based on the findings in this report, cortisone injection can be expected to provide only temporary relief from the symptoms of plantar fasciitis and is unlikely to improve long-term clinical results in the treatment of this condition.

In conclusion, this is the first study to demonstrate that platelet rich plasma can provide successful longer term treatment of severe chronic plantar fasciitis in patients who have failed to respond to traditional nonoperative management techniques. The use of PRP in these difficult situations seems far more efficacious than the traditional treatment of cortisone injection and appears safer than surgical alternatives.

Declaration of Conflicting Interests

The author declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The author is a consultant for Exactech, Inc, Gainesville, FL.

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