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Musculoskeletal Ultrasound Changes in Chronic Plantar Fascia after Treatment with Platelet Rich Plasma Compared to Steroid

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SUMMARY

Background. Chronic plantar fasciitis (PF) is a common orthopedic condition that can demonstrate hard to effectively treat. In this study, platelet-rich plasma (PRP), a concentrated bioactive blood segment wealthy in cytokines and growth factors, was compared to steroid injection in the treatment of Chronic plantar fasciitis resistant to traditional non-operative management.

Objective. To compare the effect of ultrasound-guided (US guided) injection of platelets rich plasma (PRP) with that of corticosteroid injection to treat patients with chronic PF.

Methods. Patients with PF (n = 98) were assigned to receive either PRP or corticosteroid US-guided injection with double blind randomized. The visual analogue scale (VAS) at baseline evaluated the pain level, three and twelve weeks after injection.

Results. In both corticosteroid and PRP injected groups, the average VAS heel pain scores and the mean its impact on quality of life were evaluated using the Manchester-Oxford Foot Questionnaire (MOxFQ) scores were statistically lower compared with the pre-treatment scores ($P < 0.001$). The improving symptoms in the corticosteroid group at the beginning were better and then decreased after 12 weeks; still the differences were significant, while in the PRP group symptoms progressively improved.

Conclusions. The current study results revealed that both PRP injection and corticosteroid injection are modalities for treatment of plantar fasciitis. PRP preparation is more powerful and strong than cortisone injection for the treatment of chronic plantar fasciitis, with less side effects and precautions.

Study registration. The study was registered in clinicalTrials.gov (NCT05339542).

KEY WORDS

Degenerative plantar fasciitis; heel pain; platelet rich plasma; steroid; ultrasound guided injection.

INTRODUCTION

In recent years, platelet-rich plasma (PRP) has been investigated as a treatment option for plantar fasciitis. PRP is a bioactive concentrate of various growth factors and cytokines that modulate cell proliferation and differentiation, angiogenesis, and chemotaxis (1).

When it is injected into injured tissue, the presumed mode of PRP action is to promote collagen synthesis and enhance tendon and tissue healing (2). Antonina *et al.* (3) concluded that a single injection of PRP is beneficial for the healing process in cases of Achilles rupture in experimental animals, although it was not sufficient for their functional recovery. Not surprising, long-term pain relief has been reported by a few authors, suggesting that PRP treatment augments a natural healing response (4). In theory, this makes PRP an ideal treatment option, and in fact, several studies have demonstrated very positive treatment outcome effects (5).

Various conservative treatment options include non-weight bearing, eccentric stretching, night splints, orthotics, and non-steroidal anti-inflammatory drugs. These treatment measures can resolve nearly 80% of the cases. However, in cases who are not responsive to these treatments, invasive procedures in the form of local infiltration are required. Infiltration with intra-lesional steroids is commonly used in the treatment of chronic plantar fasciitis (6, 7).

This procedure is effective, but only produces short-term relief. Moreover, it is also accompanied by complications, such as local infections, heel fat pad atrophy, and in some cases even plantar fascia rupture in case of multiple injections (7).

Platelet-rich plasma (PRP) is promoted as an ideal autologous biological blood-derived product that can be exogenously applied to various tissues, where it releases high concentrations of platelet-derived growth factors that enhance wound healing, bone healing, and tendon healing (8).

When platelets become activated, growth factors are released and initiate the body's natural healing response (9). In animals, the addition of growth factors to ruptured tendon has been shown to increase the healing of the tendon. In humans, it has been shown that the injection of platelets into the tendon decreases pain (10).

Injection of autologous platelet rich plasma (PRP) has been recently proposed as a treatment for plantar fasciitis on the evidence that it contains various growth factors and cytokines that may induce local factors to accelerate healing process (11). The autologous PRP does not have side effects compared to steroid injections. So far, PRP injections have shown promising results in various studies (12).

This prospective study makes use of the VAS score for heel pain, functional outcome scores and musculoskeletal ultrasound (MSUS) measurement of plantar fascia thickness as an outcome measure to study the actual role of single local injection of PRP in the management of plantar fasciitis (13). Literature utilizing MSUS measurement of plantar fascia thickness as an outcome measure to study the effectiveness of PRP injection are very few which makes this study unique. The null hypothesis is that PRP injection has no effect in the outcome of plantar fasciitis management (14).

The current study aimed to evaluate pain reduction with local PRP ultrasound-guided (US-guided) injections in patients with chronic PF and compare it with corticosteroid injection. In addition, to compare the effect of US guided injection of PRP with corticosteroid injection to treat chronic PF cases. The level of pain for each patient was reported by visual analogue scale (VAS) and its impact on quality of life were evaluated using the Manchester-Oxford Foot Questionnaire (MOxFQ).

PATIENTS AND METHODS

Studied population

The current single center prospective double-blind randomized clinical trial was carried out at outpatient clinic of Rheumatology Department. One hundred patients diagnosed as idiopathic PF based on the history and physical examination according to the clinical consensus statement of the American College of Foot and Ankle Surgeons (13) were involve. Two patients refused to sign the consent because of refusing the idea of corticosteroid injection, 98 conducted the study. This research was approved by the Faculty of Medicine Research Ethics Committee (FMREC), Minia University, Minia, Egypt (Approval no. 311-2022 – Date of approval: March 27, 2022) and a written consent was obtained from all participants.

Involved patients were randomly categorized into two groups. Group A included 51 patients and injected PRP. Group B included 47 patients and injected methylprednisolone (MP) serving as a (diseased control group). All patients completed the study. Patients with a history of foot trauma, interventions to the heel, neurological complaints, foot arthritis, Achilles enthesitis, foot deformity, rheumatoid arthritis, spondyloarthropathies, gout, hematological diseases or endocrinal disorders like diabetes mellitus and thyroid dysfunction and pregnancy were excluded from the study.

Clinical assessment of the severity of plantar fasciitis

Clinical evaluation pre and post injection was done by the same rheumatologist, who were blinded to the type of injection. The severity of plantar fasciitis and its impact on quality of life were evaluated using the Manchester-Oxford Foot Questionnaire (MOxFQ) and the Visual Analogue Scale (VAS) (0-10 cm). MOxFQ is a 16-item Patient-Reported Outcome (PRO) measure designed and validated for use in clinical trials involving foot disorders and surgery. These self-administered PROs can be performed to measure how foot problems affect health-related quality of life (15).

Ultrasound evaluation

A radiology consultant performed ultrasound scans pre and post injection. Using a high-frequency linear probe and power Doppler ultrasound machine Siemens Acuson P300 (10-18 MHz), Germany (16). The following parameters were identified: thickness, echogenicity, calcification, power Doppler signals, enthesophyte and cortical erosions. A MSUS EULAR certified rheumatologist with > 5 years of experience in musculoskeletal ultrasound proceeded the injection to all patients using the US-guided medial approach (17).

Platelet-rich plasma preparation

PRP was produced through whole blood centrifugation using a specific methodology in a strict aseptic setting. Then, blood was collected and mixed with anticoagulant and citrate phosphate dextrose adenine in a 10:1 blood: anticoagulant ratio. The blood was centrifuged for 10 minutes at 1000 rpm. Afterward, the plasma was transferred to a new glass tube and centrifuged for 15 minutes at 3000 rpm. At the bottom of the tube, platelets will form a pellet. Finally, pure platelet-rich plasma was obtained at a concentration of up to four times higher than baseline. Prior to the injection, calcium gluconate was combined with PRP (0.3 ml Ca gluconate/ml PRP).

Study design and the injection procedure

Blood was drawn from all participants to ensure patients blindness to the study. The injection was given under strict aseptic precautions. The area to be injected was prepared with a 10% povidone-iodine scrub and alcohol. Patients in group A (the PRP group) were injected with 3 mL PRP, whereas patients in group B (the control group) were given 2 ml (40 mg) MP with 1 ml of 2% lidocaine hydrochloride. All injection procedures were performed under continuous US imaging. A 22-gauge needle was introduced from the medial approach to reach the proximal insertion of the plantar fascia, and injection of the PRP or MP was given. Immediately after injection, the patients were observed for 30 minutes and discharged. They were advised to rest and avoid high-impact activities for the following three days. Subsequently, they can resume their ordinal activities. Patients were allowed to take paracetamol for pain after the injection. Additional treatments such as a splint, oral non-steroidal anti-inflammatory drugs, and any foot orthosis were not allowed during the study. Twelve weeks later, all patients were re-assessed clinically and sonographically by the same investigator.

Statistical analysis

Data entry and data analysis were done using SPSS version 25 (Statistical Package for Social Science). Data were presented as number, percentage, mean, standard deviation. Chi-square test was used to compare between qualitative variables. Independent sample t-test was used to compare quantitative variables between groups. Using paired t test to compare between numeric variables with follow-up in the same group. P-value considered statistically significant when $p < 0.05$.

RESULTS

Baseline clinical characteristics and assessment of the study population

A total of 98 patients with PF (54.1% males, 45.9 % females) were included in this study. The mean age was 45.1 ± 6.2 (32-58) years. The duration of illness ranged from 3-9 months with a mean of 4.8 ± 1.4 months, and their BMI was 24 ± 2.9 kg/m^2.

Table I shows fifty-one PF patients, 25 males (49%) and 26 females (51%), with a mean age of 44.9 ± 5.6, ranging between 33-58 years, and a mean disease duration of 4.6 ± 1.3, 3-8 months. Their BMI was 23.7 ± 2.9, 18.6-30.1 kg/m^2. Patients in the control group were matching in terms of sex (28 males 59.6% and 19 females 40.4%), age (45.2 ± 6.7, 32-58 years), disease duration (5 ± 1.5, 3-9 months) and BMI (24.4 ± 3, 17.6-29.6 kg/m^2).

At baseline assessment, no significant difference was detected between groups regarding VAS ($p = 0.26$), MOxFQ ($p = 0.2$), duration of illness ($p = 0.15$).

Table II and **figure 1** summarize the ultrasonography findings in all patients at baseline. US evaluation; thickness ($p = 0.07$), calcifications ($p = 0.2$) and erosions ($p = 0.7$). All patient heels were hypoechoic (100%). No Doppler signal was detected from any of the examined heels. Upon follow-up there was highly significant difference ($p < 0.000$) in Thickness, Echogenicity and Calcification, but there was non-significant different in follow-up in erosions.

Follow-up evaluation of the VAS and MOxFQ study patients

As illustrated in **table III** and **figure 2**, after a 12-week follow-up, the PRP group demonstrated a significant reduc-

Table I. Demographic data and clinical data at baseline in study groups.

Item	Group A PRP n = 51	Group B MP n = 47	P-value
Age, years	44.88 ± 5.64 (33.0-58.0)	45.23 ± 6.72 (32.0-58.0)	0.779
Sex, M:F	25 (49.0%):26 (51%)	28 (59.6%):19 (40.4%)	0.199
BMI, Kg/m^2	23.73 ± 2.87 (18.8-30.1)	24.37 ± 2.98 (17.6-29.6)	0.283
Disease duration, months	4.62 ± 1.32 (3.0-8.0)	5.04 ± 1.53 (3.0-9.0)	0.154
VAS at baseline	8.16 ± 73 (7.0-9.0)	7.95 ± 0.99 (6.0-9.0)	0.260
MOxFQ at baseline	77.6 2 ± 9.0 (60.0-95.0)	75.21 ± 9.67 (60.0-90.0)	0.203

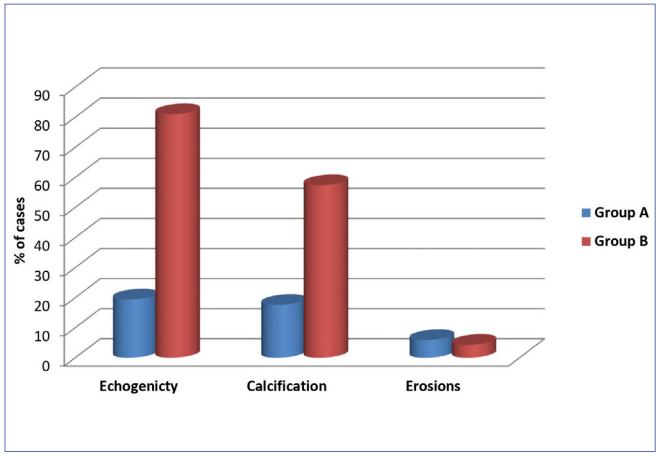

Figure 1. Ultrasound data at follow-up in study groups.

% of cases in group A (PRP), Group B (MP) with ultrasound data "Echogenicity, Calcification & Erosions" with highly significant difference ($p < 0.000$) between group A&B with each of Echogenicity, Calcification, on other side there was non-significant difference between group A and B with Erosion using Qui-square test.

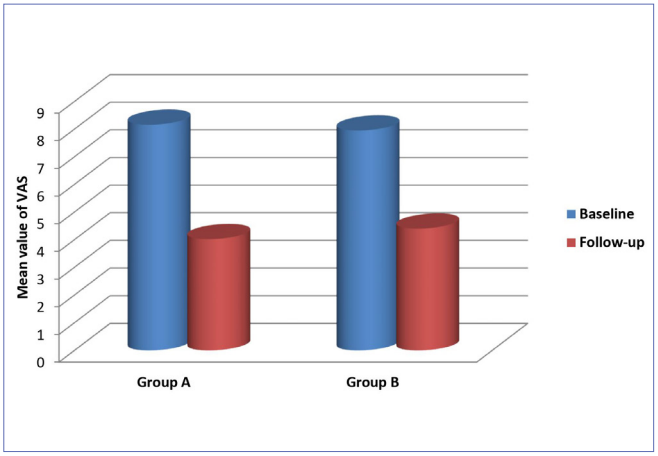

Figure 2. VAS at baseline and follow-up in study groups.

Mean value of VAS, Group A (MP), Group B (PRP) comparison between mean value of VAS at baseline and after follow-up in group A and B, with highly significant difference ($p < 0.000$) at follow-up "independent t-test". In group A there was highly significant difference ($p < 0.000$) between baseline and follow-up, moderate significant difference ($p < 0.001$) in group B (MP) "Paired T-test".

Table II. Ultrasound data and at baseline and follow-up in study groups.

Item	Group A PRP n = 51	Group B MP n = 47	P-value
Thickness at baseline	8.27 ± 0.87 (7.0-12.0)	7.95 ± 0.87 (5.9-9.1)	0.07
Thickness at follow-up	4.05 ± 0.44*** (3.0-5.0)	6.47 ± 1.27** (3.5-8.0)	0.000***
Echogenicity at baseline	51 (100%)	47 (100%)	---
Echogenicity at follow-up	15 (19.4%)***	38 (81.0%)	0.000***
Calcification at baseline	25 (49.0%)	29 (61.7%)	0.145
Calcification at follow-up	9 (17.6%)***	27 (57.4%)	0.000***
Erosions at baseline	3 (5.9%)	2 (4.3%)	0.539
Erosions at follow-up	3 (5.9%)	2 (4.3%)	0.539
Heel fat pad thickness mm	13.42 ± 3.74 (7.90-23.10)	14.30 ± 3.81 (7.80-23.50)	0.255

Table III. Outcome data and at baseline and follow-up in study groups.

Item	Group A PRP n = 51	Group B MP n = 47	P-value
VAS at baseline	8.16 ± 73 (7.0-9.0)	7.95 ± 0.99 (6.0-9.0)	0.260
VAS at follow-up	4.02 ± 1.21*** (0.0-10.0)	5.14 ± 1.81** (1.0-7.0)	0.000***
Change in VAS	4.13 ± 2.06	2.81 ± 1.74	0.001**
% change	50.24%	35.35%	
MOxFQ at baseline	77.62 ± 9.0 (60.0-95.0)	75.21 ± 9.67 (60.0-90.0)	0.203
MOxFQ at follow-up	25.11 ± 9.90*** (10.0-42.0)	29.95 ± 11.50*** (10.0-56.0)	0.028*
Change in MOxFQ	52.50 ± 11.27	45.25 ± 15.75	0.02*
% change	67.61%	59.33%	

Table IV. Change in thickness at baseline and follow-up in study groups.

Item	Group A PRP n = 51	Group BMP n = 47	P-value
Thickness at baseline			
≤ 4	0	0	--
> 4	51 (100%)	47 (100%)	
Thickness at follow-up			
≤ 4	32 (62.7%)	5 (10.6%)	0.000***
> 4	19 (37.3%)	42 (89.4%)	

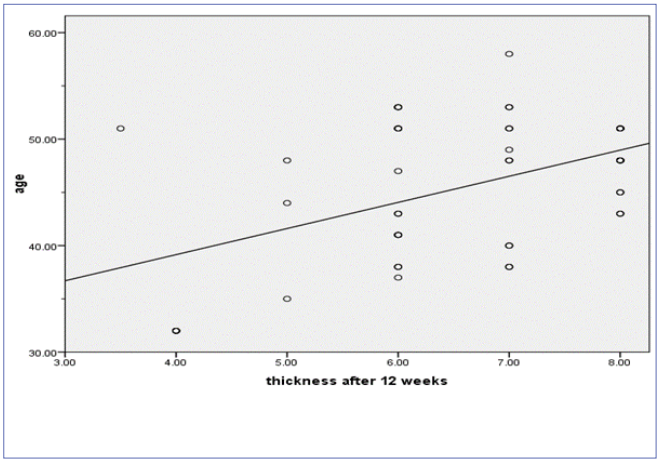

Figure 3. Correlation between thickness after 12 weeks and age in MP group.

There was positive correlation between thickness after 12 weeks and age (r = 0.352, p < 0.015*).

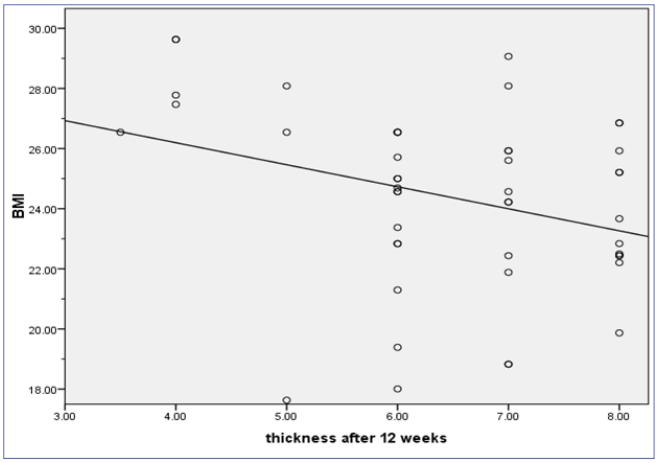

Figure 4. Correlation between thickness after 12 weeks and BMI in MP group.

There was negative correlation between thickness after 12 weeks and BMI (r = -0.312, p < 0.03*).

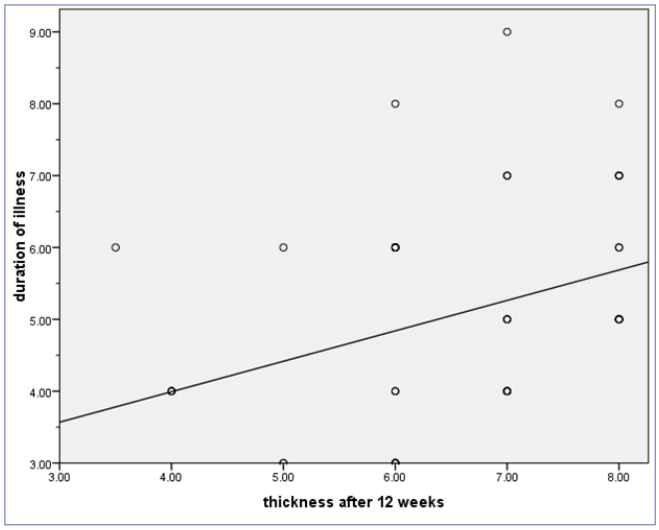

Figure 5. Correlation between thickness after 12 weeks and duration of illness in MP group.

There was negative correlation between thickness after 12 weeks and duration of illness (r = 0.464, p < 0.001**).

tion in the VAS with highly significant different (p = 0.000) and there was significant different in MOxFQ compared to the MP group with percentage change (50.24%) in PRP group *vs* 35.35% in MP group.

In **table IV** in PRP group, thickness ≤ 4 was 32 (62.7%) from 51 patients. In MP group there was 5 (10.6%) patients from 47 patients. With highly significant difference (p < 0.000).

In MP group there was negative correlation between PF thickness and BMI (r = -0.312, p < 0.03) and there was positive correlation between thickness with each of age and duration of illness, respectively (r = 0.352, p < 0.015; r = 0.464, p < 0.001) (**figures 3-5**). In PRP there was no correlation between thickness with each of BMI, duration of illness and age.

DISCUSSION

The purpose of this randomized study was to examine the efficacy of PRP *versus* corticosteroid injections for treating chronic plantar fasciitis. For persistent recalcitrant plantar fasciitis that does not respond to non-operative treatment, there is no accepted standard of care management. Since plantar fasciitis is a degenerative condition, several experts think that PRP's ability to promote regeneration may be helpful. A non-operative therapeutic option for a degenerative tendon disease may involve injecting concentrated autologous platelets.

In cases where conservative approaches fail to offer relief, injectable therapy has been proposed as a second line of treatment (6). They are believed to lessen inflammation and pain, which will improve functionality. Infection, atrophy of the fat pad, and in some cases even rupture of the plantar fascia have all been linked to the mainstay of this treatment, steroid injections (18).

Plantar fasciitis was previously thought to be purely an inflammatory condition; however, recent evidence suggests primarily a degenerative pathology (1). This degeneration of the plantar fascia is thought to be because of microtears, which in turn contribute to recurrent inflammation, further microtears, and a cycle of degenerative inflammation. Histologically, plantar fasciitis demonstrates myxoid degeneration, disorientation of collagen fibers, and collagen necrosis similar to tendinopathy (19).

While both PRP and CS can decrease inflammation, PRP may be advantageous over CS as it may modulate the plantar fascia degeneration because of its biological regenerative properties. PRP contains an abundance of growth factors and bioactive cytokines, which are believed to influence healing by augmenting cellular migration, improving cellular proliferation, promoting angiogenesis, and increasing matrix deposition (20).

This results in increasing fiber organization and tensile strength in soft tissue (21). PRP also releases vascular endothelial growth factor, which promotes angiogenesis and may facilitate healing of degenerative condition by improving neovascularization and repair. By contrast, CS has no such regenerative capacity, and consequently its effect will be solely in reducing inflammation and thus is short-lived (22).

A research concluded that patients with plantar fasciitis have thicker plantar fascia than those without heel discomfort. In plantar fasciitis, the appearance of the plantar fascia on ultrasonic examination revealed inflammatory alterations (23) while another research adds to our understanding of functional stability in the medial column of the foot (24).

The current study used US-guided injection. There is evidence that US-guided plantar fascia injection can help with a reduction in plantar fascia thickness and pain; also, there was no evidence of the rupture in plantar fascia at follow-up ultrasound examination; therefore, in some studies US-guided injection is suggested (25).

While there are many studies in which PRP injection to treat chronic PF is beneficial, it is a controversial issue. Aksahin *et al.* (26) in their prospective, randomized controlled trial compared corticosteroid and PRP injections to treat PF reported that both methods impressively treated PF.

Our finding in study investigation with ultrasound there was improvement in ultrasonography parameters in group A PRP than group B Methylprednisolone with highly significant difference ($p < 0.000$). This agrees with Homayouni *et al.* (27) who reported the current study used US-guided injection. There is evidence that US-guided plantar fascia injection can help with a reduction in plantar fascia thickness and pain.

Our findings suggest that PRP was associated with greater improvement in VAS score. More percent change in VAS score in PRP group than steroid group with moderate significance ($p < 0.001$) was observed, and resulted in superior score at 3 months compared to steroid injection. Aksahin *et al.* (26), Jain *et al.* (28) and some other studies observed entirely different results. In the study of Shetty *et al.* (29), the authors compared the efficacy of corticosteroid injection (30 patients) with PRP injection (30 patients).

At the 3-month follow-up, the post-injection measure outcomes were significantly improved in both groups. In addition, these results were much better in the PRP group than that in the steroid group. Similarly, Say *et al.* (30) compared the effects of PRP and steroid in patients with plantar fasciitis. The authors assessed 50 patients divided among each group.

PRP had a larger change in MOxFQ and VAS scores than that in the steroid group, both at 3 months. Concerning the long-term effect of PRP, our results suggested that PRP was associated with greater changes in VAS and MOxFQ scores compared to local steroid injections at 3 months. Likewise, in the study of Monto (31), difference in AOFAS and VAS score between the PRP and steroid groups was clinically significant at the 12- and 24-month follow-up evaluations ($p < 0.001$).

According to our research, the PRP group experienced a 50% improved decrease in VAS score over the follow-up period compared to the MP group's 35.35%. This is consistent with Peerbooms *et al.* (9), who observed that more patients in the PRP group (84.8%) demonstrated at least a 25% improvement in pain score between the baseline and the 1-year follow-up than in the control group (55.6%). Our results in this study, which showed a reduction in pain and disability following a PRP injection, were well compared with other published studies on the treatment of plantar fasciitis (32).

In our results there was improvement of thickness after follow-up ≤ 4 in PRP into (62.5%) *vs* (10.6%) in MP group with highly significant difference ($p < 0.000$). This agrees with Perez, *et al.* (33). Studies have shown a significant reduction in plantar fascia thickness after PRP injection. Plantar fascia thickness in both the PRP group and corticosteroid group were comparable prior to injection. However, at six months follow-up, the PRP group had a significant reduction (35.45%) in the thickness of plantar fascia compared to corticosteroid group (29.16%). The difference between the two groups was statistically significant (33). The increase of the plantar fascia thickness is in positive correlation to the clinical outcome (34). In our study there was positive correlation between PF thickness and pain score "VAS" after 12 weeks of treatment in MP treatment. This agree with Lai *et al.* (35) who reported there was positively correlated with the decrease of VAS score at 12th week follow-up. Also, our results indicate that functional recovery (in terms of MOxFQ scores) is not correlated with baseline fascial thickness, nor with the degree of fascial thinning after treatment, regardless of treatment modality (36).

From regression analysis there was significant relation between age, BMI, and duration of illness with decrease thickness in follow-up in MP group. On other side there was no relation between age, BMI and duration of illness with thickness at follow-up in PRP group that became more advanced in using PRP which give more chance in using. Moreover, our study was in concordance with Vahdatpour *et al.* (37) who stated that PRP has more efficacies over the local steroid injection treatment. Also Jiménez-Pérez *et al.* (38) reported Injections of PRP is a safe, more efficient and long-lasting method than that of corticoid injections. Injections of PRP produce a significant clinical improvement that is maintained in time and MRI and US have proven useful in assessing the response of plantar fascia injuries to non-operative treatments.

Without any notable local or systemic side effects, all trial participants tolerated the local PRP injection. The study's limitations were a limited sample population and a brief follow-up period. RCT with a bigger research population and a longer follow-up will be beneficial in better understanding the long-term advantages and efficacy of the PRP injection in the management of persistent plantar fasciitis, which will help to address the limitations of this study.

CONCLUSIONS

The results of this study indicate that short-term improvements in VAS scores for heel pain, functional outcome scores, and restoration of plantar fascia thickness in patients with chronic plantar fasciitis showed clinically and statistically significant improvements. This was supported by US measurements. According to the study, local PRP injection is an efficient and safe treatment for chronic plantar fasciitis. Our study expands on the previous studies to provide a better evidence for superiority of PRP over local injection of steroid in plantar fasciitis, and the authors conclude that PRP provides better pain relief and function as compared to steroid injection.

FUNDINGS

None.

DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

AEH, SAS, SR: study trial performance. AEH, SAS: data analyses. MAA: patients' PRP samples preparation. AEH, FMI, SAS: study design, data review. AEH, SAS: manuscript writing. All authors reviewed the manuscript and concurred with the findings.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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