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Analgesic efficacy and functional outcome in refractory cases of plantar fasciitis treated with platelet-rich plasma: randomized comparative study with corticosteroids injection

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ABSTRACT

Background: Steroid injection is a widespread treatment for plantar fasciitis but seems to be useful to a lesser extent, Platelet-rich Plasma (PRP) injections into the plantar fascia start the healing process required to stop the degeneration of the plantar fascia at its root.

Aim of the study: To compare analgesic efficacy, functional outcome, degree of satisfaction and improvement of fascial thickness and echogenicity after platelet-rich plasma injection versus corticosteroids injection in refractory cases of plantar fasciitis.

Patients & method: 60 patients with refractory plantar fasciitis who were resistant to conservative treatment were randomized to receive either PRP or steroid injection. All patients were assessed with the American Orthopaedic Foot and Ankle Society (AOFAS) score, Visual Analogue Score (VAS) for pain, the Roles-Maudsley (RM) Score and plantar fascia thickness and echogenicity. Data were collected prospectively, pre-treatment, at 3, 6, 12 week, and 6 months post-injection.

Results: There was significant improvement in both groups as regards the clinical outcome measures involving (VAS & AOFAS) and radiological outcome measures including (thickness and echogenicity) in all post-injection times. However, steroid group showed early improvement (at 3rd week post-injection) with short duration while PRP group showed improvement at 12 weeks post-injection till the end of the study.

Conclusion: The use of PRP injection is safer with better analgesia and functional outcome than steroid therapy for treating chronic plantar fasciitis.

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Plantar fasciitis; Platelet-rich plasma; corticosteroids

1. Introduction

Plantar fasciitis is a typical reason for heel pain in grown-ups. It is reported that more than one million patients seek for treatment every year for this condition, Plantar fasciitis is believed to be brought about by biomechanical abuse from delayed standing or running, along these lines making microtears at the calcaneal enthesis [1,2]. A few specialists have defined this condition “plantar fasciosis”, inferring that its etiology is a more chronic degenerative process versus acute inflammation [2,3].

Non-operative therapy is typically the initial line of treatment for plantar fasciitis including rest, ice application, stretching, proper footwear, arch supports, orthotics, night splints, extracorporeal shockwave therapy (ESWT) and anti-inflammatory agents. This type of non-operative treatment is successful in up to 90% of patients complaining this condition. However, in cases who are not responsive to these treatments, invasive procedures are required. Infiltration with intralesional steroids is mostly used in chronic plantar fasciitis treatment [4]. This procedure is effective, but only has short-term pain relief [5].

Since corticosteroids have a potent anti-inflammatory impact, they help hasten the pain-relieving process. However, plantar fascia rupture, infection, skin pigmentation, muscular damage, post-injection flares, and fat pad atrophy can all be brought on by corticosteroid injections used to treat plantar fasciitis [6]. Another treatment alternative is platelet-rich plasma (PRP) injection. Autologous PRP therapy is not recent. The healing pathway, which is the physiological reaction to any injury or surgical procedure, is well documented and depends on proteins that are migrated to the healing site through platelets and white blood cells with proteins that are present in the plasma [7].

Platelet-rich plasma (PRP) is a concentrate of platelets, which are a source of autologous growth factors. The cytokines present in the α-granules of the platelets have been shown to enhance fibroblast migration and proliferation, upregulate vascularization, and enhance

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collagen deposition in a variety of settings [7]. Accordingly, PRP injection into the damaged tissue should enhance healing and counter the degenerative processes occuring in the origin of the plantar fascia.

Although numerous studies have been documented success in the healing of tissues, and the Current evidence has shown great outcome of PRP in treating plantar fasciitis [8,9]. However, whether it is more efficient in decreasing pain and improving function than other treatments (e.g., steroid injection or whole blood) remains controversial. Therefore, the purpose of this prospective study was to compare analgesic efficacy & functional outcome of platelet-rich plasma injection versus corticosteroids injection in refractory cases of plantar fasciitis.

2. Patients and method

A randomized prospective double-blinded study was carried out in pain management clinics, Faculty of Medicine, Zagazig University with duration of nearly a year (from November 2021 to November 2022). Patients were allocated randomly using computer-generated random table into two equal groups, 30 cases each (PRP group & steroid group).

Patients aged 21–60 years old of ASA I & II with body mass index less than 35 Kg/M^2 with unilateral refractory chronic heel pain due to plantar fasciitis not responding to conservative (medical & physical) treatment more than 3 months were included in the study. While those with systemic disease e.g., Diabetes mellitus, active tumor, hematological malignancy, infection, history of using anticoagulants, Hb values$^<$7 g/dL, thrombocytic count $^<$150,000/mm^3, previous steroid injection into the heel or ESWT therapy, history of calcaneus fracture or surgery and mental disorders were excluded. In addition, pregnant patients were excluded.

The present prospective clinical study was conducted after obtaining approval from the local ethics committee and Institutional Research Board (IRB) under the approval number of (8057). All participants in this study provided written informed consent, following the guidelines of the Declaration of Helsinki. The patients included in this study were those diagnosed with chronic plantar fasciitis and were monitored for at least 3 months. Injection was considered for those patients who failed to respond to conservative treatment and stretching exercises.

In order to diagnose plantar fasciitis, history and a clinical examination were performed, and radiographs were conducted to eliminate the possibility of other heel pathologies.

2.1. PRP preparation

Platelet-rich plasma was prepared and applied under the same conditions using the method described by Dhurat and Sukesh [10]. A total of 10 cc peripheral blood were obtained from the antecubital region. The blood is collected on citrated tube and mixed with 3.2% sodium citrate by inversion. By using centrifugation equipment (Nahita centrifuge made in Spain with 16 tubes capacity & up to 5000 r.p.m) The tubes were centrifuged (first centrifugation), the rotation speed and time was (3000 rpm × 3 minutes) at room temperature, sample separated into red blood cells (RBCs) in the bottom, middle thin layer containing white cells (puffy coat) and the upper layer containing plasma. The tubes were taken out from the centrifuge and arranged on a holder then the plasma & puffy coat were aspirated by syringes and collected in another sterile tube without anticoagulant and was centrifuged (second centrifugation). The plasma tube underwent second centrifugation at 4000 rpm for 15 minutes. Plasma separated into two layers; platelet-rich plasma (PRP) with platelet pellets at the bottom and platelet-poor plasma (PPP) on the top. Platelet pellets were suspended by gently shaking the tube after the supernatant platelet-poor plasma (PPP) was removed, leaving 2.5 ml of PRP [10]. The PRP sample activated by 125 ul of 0.025 calcium chloride (CaCl2).

2.2. US-guided injection technique

- Patient lied in supine position.
- Skin of the heel was sterilized with betadine.

The site of injection was infiltrated with 2 ml of xylocaine 2% just before injection.

In the PRP group, 2.5 ml of PRP mixed with 2.5% calcium chloride ($CaCl_2$) (50 µl of $CaCl_2$/ml of PRP) was injected.

In the steroid group, a combination of 1 ml of 40 mg/ml of methylprednisolone and 1 ml of xylocaine 2% was applied.

Both steroid and PRP syringes were prepared by assistant doctor and covered with adhesive non transparent tape and given to investigator ready for direct injection under supervision of expert anesthesiologist, with a 6-year experience of musculoskeletal ultrasound (double blinded technique).

Ultrasound-guided injection technique was used in both groups. The injection was performed using a medial approach of the heel with US superficial probe (with a 4–11 MHz linear transducer VF10–5; Siemens Setting transducer frequency at 7.5 MHz) placed on the most tender point of the heel parallel to longitudinal axis of the foot to visualize plantar fascia and site of injection. A 22-gauge needle was directed into the center of the hypoechoic plantar fascia (out of plane). The dispersal of the injection mixture into the structure of the plantar fascia was shown on post-injection ultrasound under sterile conditions. The patient stayed in the supine position for

20 minutes following administration. For the first 24 hours after injection, patients were instructed to lay down and avoid standing.

2.3. Post-injection analgesic protocol

The use of NSAID or foot orthoses was prohibited. Because there may be discomfort felt at the site of the injection for up to 72 h. Patients were advised to ice the injection site, elevate the limb, and modulate activities. The patients were instructed to remain seated for 15 minutes following injection without getting up. Patients were sent home with instructions to limit their activities for 48 hours. Patients were advised to take acetaminophen (paracetamol) as an analgesic for post-injection pain relief (pain related to injection which occurred immediately after injection and extended up to 96 hours and along course of follow-up). According to (VAS), paracetamol 500 mg 1 tablet/8 hours in mild pain (VAS 1–3), 1 tablet/6 hours in moderate pain (VAS 4–6)& 1 tablet/4 hours with maximum dose 4 grams (8 tablets) a day in severe pain (VAS 7–10) [11]. After 2 days, patients visited the physiotherapist to start stretching exercises for 2 weeks for the Achilles tendon and the plantar fascia to all patients. Four weeks post-injection, the patients were free to start normal recreational activities [12].

Clinical evaluation was done pre-treatment and at intervals of 3,6,12 weeks and 6 months follow-ups. The American Foot and Ankle Score(AOFAS) [13] and the visual analog scale(VAS) were used in the clinical assessment. VAS was 0–10 cm line (0= no pain, 1–3= mild pain, 4–6= moderate pain, 7–10= severe pain) [14]. Patients were evaluated also regarding to side effects (increased pain for more than 72 hours following the injection, infection, and heel fat pad atrophy) and subjective satisfaction. The modified criteria of the Roles and Maudsley score was used in rating satisfaction [15]. The grades of this scale were: excellent (no pain, patient satisfied with the treatment outcome, and unlimited walking without pain), good (symptoms substantially decreased, patient satisfied with the treatment outcome, with painless walk for >1 h), acceptable (symptoms somewhat decreased, tolerable pain than pre-treatment, and patient slightly satisfied with the treatment outcome), or poor (symptoms similar or worse and patient not satisfied with the treatment outcome). Improvement of plantar fascia thickness and echogenicity pre & post-injection were also assessed in follow-up.

2.4. Patient outcome

2.4.1. 1ry outcome

1. American foot and ankle score (AOFAS): the AOFAS evaluation covered pain (40 points), function (maximum walking distance, walking surfaces, gait abnormality, sagittal motion, hindfoot motion)(40 points) and alignment (10 points) [13].

(a) A score of 90–100 points was considered excellent.
(b) A score of 80–89 points was considered good.
(c) A score of 70–79 points was considered fair.
(d) A score of less than 70 points was considered poor.

2. Visual analog score (VAS): VAS was used in the clinical evaluation.

2.4.2. 2ry outcome

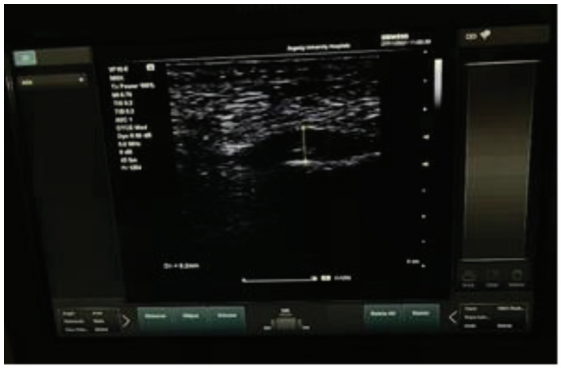
(1) US-guided evaluation of plantar fascia diameter and echogenicity (On a longitudinal view of the heel, starting at the frontal margin of the inferior calcaneal border, the maximal thickness of the plantar fascia was measured). In plantar fasciitis there is marked thickening of the plantar fascia e.g., more than 4 mm in association with diminished echogenicity, loss of fascial boundary definition distal to calcaneal insertion, or both [16] (**Figure** 1 & Figure 2).
(2) Patient's satisfaction (modified criteria of the Roles and Maudsley score).
(3) Post-injection side effects e.g., hematoma, bruises, infection or heel fat pad atrophy [17].

2.5. Sample size

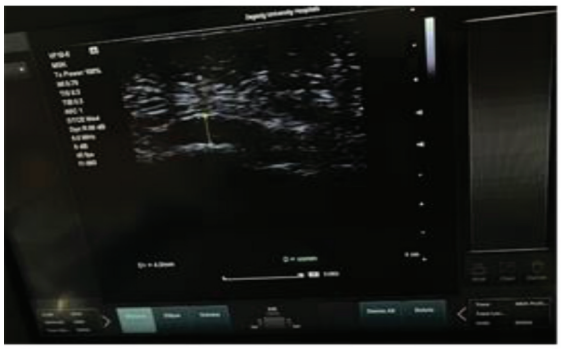
Based on data from (Soraganvi et al., 2019) [18], which compared AOFAS in PRP Vs steroid group, the effect size was 15.36. With a significant criterion of $\alpha = 0.05$and power = 1, a sample size of ($N = 60$), 30 cases per group, taking into account 10% dropout rate, is more than adequate to test the study hypothesis.

2.6. Statistical Analysis

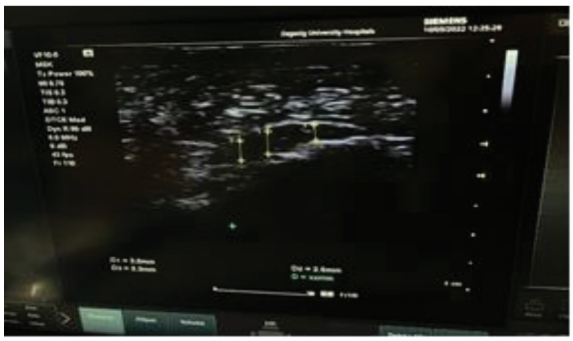
i. Statistical package for Social Science **(SPSS 25)** was used to review, code, tabulate, and introduce the acquired data to a computer. Data were given, and the type of data gathered for each parameter was appropriately analyzed. **Descriptive statistics**: Mean, Standard deviation (± SD) and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data.Frequency and percentage of non-numerical data. **Analytical statistics**: Student T Test, Fisher's exact test, Chi-Square test, General linear model (GLM), The Cochran Q procedure, ANOVA test, Post Hoc Test, Linear regression to test and estimate the dependence of a quantitative variable based on its relationship with a set of independent variables and Marginal homogeneity test assess the statistical significance of the difference of a variable with multiple categories



(1) pre-injection (thickness=6.2mm)

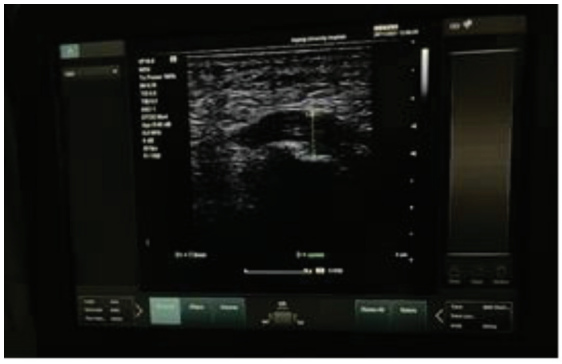


(2) 6w post PRP injection (thickness=5.7mm)

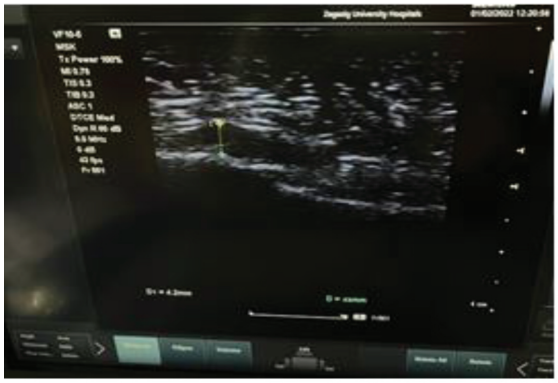


(3) 6m post PRP injection (thickness=3.2mm)

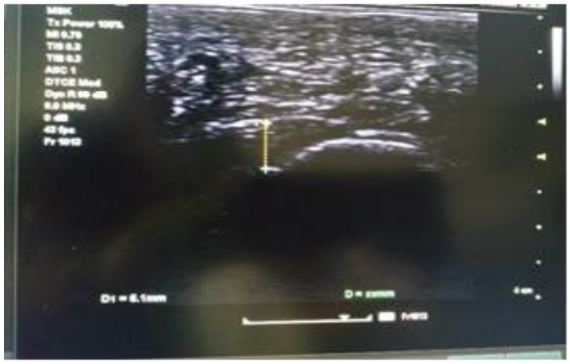
Figure 1. US-guided pre- & post-PRP injection follow up of fascia thickness..



(1) pre-injection (thickness=7.8mm)



(2) 6w post steroid injection (thickness=4.2mm)



(3) 6m post PRP injection (thickness=6.1mm)

Figure 2. US-guided pre- & post-steroid injection follow up of fascia thickness..

measured twice for the same study group considering p-Value was significant at < 0.05.

3. Results

Seventy-two patients with refractory plantar fasciitis scheduled for injection of plantar fascia. Twelve patients were excluded from the study because they were not meeting the inclusion criteria ($n = 7$) and refusing to participate ($n = 5$). Finally, 60 patients completed the study (Figure 3).

There was statistically nonsignificant difference between the two studied groups as regarding the demographic data (age, BMI, sex, medical history, ASA classification and history of physiotherapy) and duration of heel pain pre-injection (Table 1).

Patients injected with PRP showed duration of post-injection pain of 74.4 ± 7.32 hours and all patients need post-injection analgesia (100%) while patients received steroid injection reported no post-injection pain (0% need post-injection analgesia) (Table 1).

Steroid group showed improvement in VAS and AOFAS scores in a descending manner being better early (3 weeks) post-injection and improvement decreased with time. While in PRP group, the improvement was in an ascending manner being of

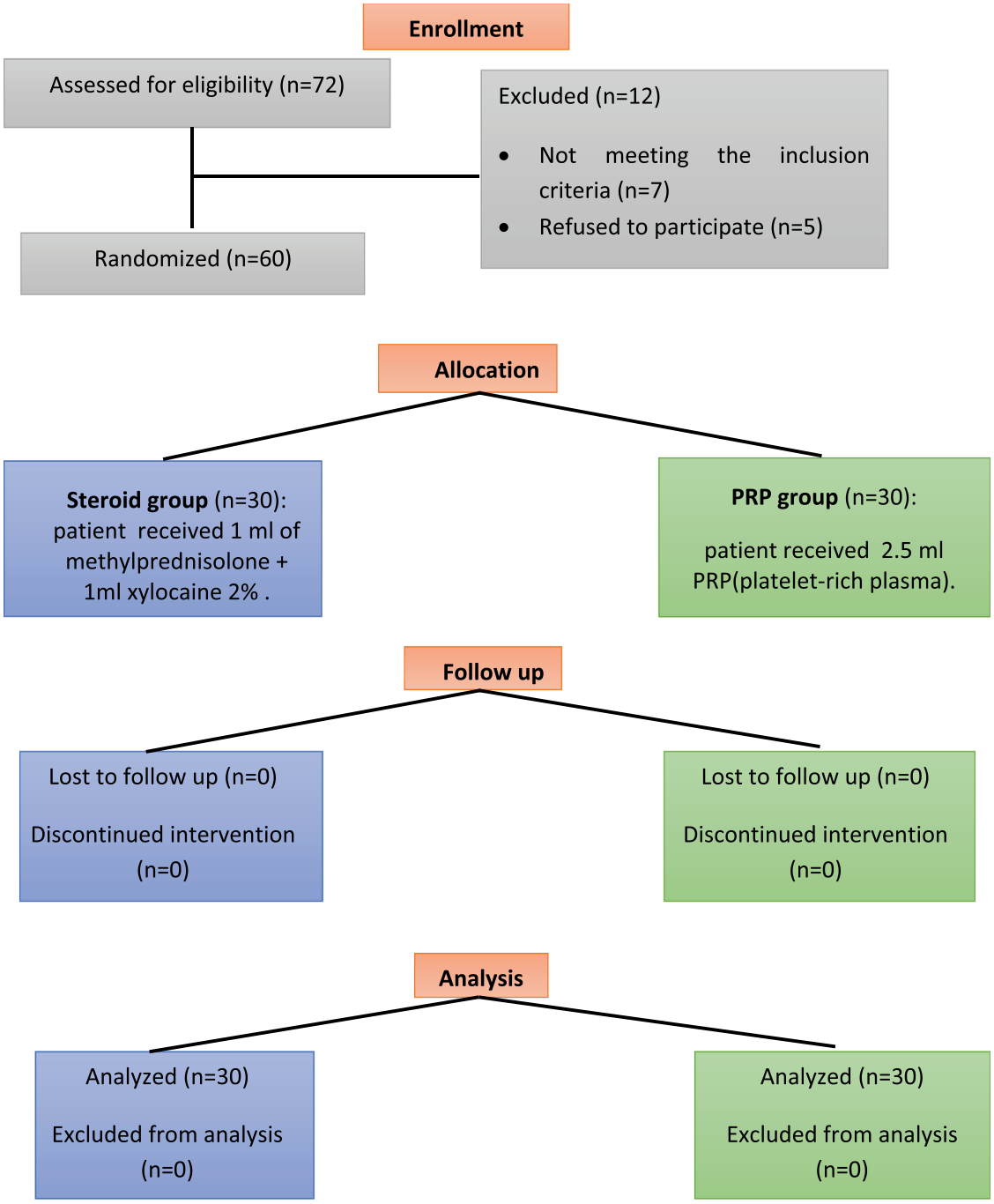


Figure 3. Flow chart of the study.

late onset (6 weeks) post-injection and improvement increased with time. There was statistically highly significant difference as regarding VAS and AOFAS scores between the two studied groups at 3, 12 weeks and 6 months post-injection while at 6 weeks post injection the difference was non significant (Tables 2,3).

Diameter of plantar fascia showed improvement in both groups with statistically significant decrease in PRP group than steroid group at 3, 12 weeks and 6 months post injection (mean 6.48 ± 0.74, 5 ± 0.69, 4.87 ± 0.71 mm in PRP group Vs 5.64 ± 0.63, 6.01 ± 0.55, 6 ± 0.56 mm in steroid group). While 6 weeks post-injection the difference was non-significant (5.86 ± 0.68 & 5.74 ± 0.66 mm in PRP & steroid groups, respectively) (Table 4).

Regarding the correlation between duration of heel pain, percentage of change in AOFAS (at 6 weeks & 6 months) and percentage of change in diameter of fascia (at 6 weeks & 6 months) within each group, there was non significant correlation between duration of heel pain and percentage of change of either AOFAS score or diameter of fascia. However, at 6 weeks, there was a significant moderate negative correlation between percentage of change in AOFAS and percentage of change in diameter of fascia within PRP group only (r−0.516). while at 6 months there was significant strong negative correlation between percentage of

Table 1. Demographic data with pre and post-treatment evaluation of the two studied groups.

		Drug used		Test of significance	
		PRP (*N*= 30) Mean ± SD	Steroids (*N*= 30) Mean ± SD	p-Value	Sig.
	Age (years)	46.67 ± 6.33	44.4 ± 7.36	0.206**(T)**	NS
	BMI (kg/m^2)	31.03 ± 2.36	31.77 ± 2.27	0.224**(T)**	NS
		n (%)	**n (%)**		
Sex	Male	9 (30%)	4 (13.33%)	0.117**(C)**	NS
	Female	21 (70%)	26 (86.67%)		
ASA	I	25 (83.33%)	26 (86.67%)	1.00**(F)**	NS
	II	5 (16.67%)	4 (13.33%)		
		Mean ± SD	**Mean ± SD**		
Duration of heel pain (months)		10.9 ± 4.42	10.9 ± 4.42	1.00**(T)**	NS
Duration of pain post-injection (hours)		74.4 ± 7.32	0 ± 0	<0.001****(T)**	HS

Data were expressed as mean±standard deviation (SD), number (n) & percentage (%), Platelet-rich plasma(PRP), body mass index(BMI) , American society of anethesiologists(ASA), (T) t-test of significance, (C) Chi-Square test of significance, (F) Fisher's Exact test of significance, non-significant(NS), ** highly significant(HS).

Table 2. VAS between the two studied groups.

			Drug used		Student t-test	
			PRP (*N*= 30)	Steroids (*N*= 30)	p-Value	Sig.
VAS	Pre-injection	Mean ± SD	7.87 ± 0.63	7.83 ± 0.7	0.847	NS
		Median (IQR)	8 [7,8]	8 [7,8]		
	3w post-injection	Mean ± SD	6.13 ± 0.9	4.1 ± 1.37	<0.001**	HS
		Median (IQR)	6 [5–7]	4 [3–5]		
		% of change	−22.80%	−47.60%		
	6w post-injection	Mean ± SD	4.4 ± 1.33	4.8 ± 1.61	0.298	NS
		Median (IQR)	4 [4,5]	4 [3–7]		
		% of change	−44.30%	−38.70%		
	12w post-injection	Mean ± SD	3.23 ± 2.19	5.63 ± 1.25	<0.001**	HS
		Median (IQR)	2 [2,3]	5.5 [5] - [7]		
		% of change	−59.50%	−28.50%		
	6m post-Injection	Mean ± SD	3.5 ± 2.16	5.97 ± 1.1	<0.001**	HS
		Median (IQR)	3 [2,3]	6 [6,7]		
		% of change	−55.70%	−23.40%		

Data were expressed as mean±standard deviation (SD), median, interquartile range(IQR), number (n) & percentage (%), Platelet-rich plasma(PRP), visual analog score(VAS), (T) t-test of significance, (C) Chi-Square test of significance, (F) Fisher's Exact test of significance, non-significant(NS), p<0.001** highly significant(HS)..

Table 3. AOFAS between the two studied groups.

			Drug used		Student t-test	
			PRP (N= 30)	Steroids (N= 30)	p-Value	Sig.
AOFAS score	Pre-injection	Mean ± SD	47.47 ± 5.62	47.87 ± 5.96	0.79	NS
		Median (IQR)	49 (44 - 52)	49 (44 - 52)		
	3w post-Injection	Mean ± SD	63.37 ± 7.62	77.97 ± 11.88		
		Median (IQR)	65 (60 - 66)	84 (65 - 87)	<0.001**	HS
		% of change	33.5%	62.8%		
	6w post-injection	Mean ± SD	77.8 ± 10.63	74.67 ± 13.31		
		Median (IQR)	80 (75 - 85)	79 (60 - 85)	0.318	NS
		% of change	63.8%	55.9%		
	12w post-injection	Mean ± SD	85.3 ± 15.15	68.2 ± 11.42		
		Median (IQR)	92 (88 - 94)	68 (56 - 78)	<0.001**	HS
		% of change	79.6%	42.4%		
	6m post-injection	Mean ± SD	83.67 ± 15.91	63.6 ± 9.72		
		Median (IQR)	90.5 (87 - 92)	61 (56 - 68)	<0.001**	HS
		% of change	76.20%	32.80%		

Data were expressed as mean±standard deviation (SD), median, interquartile range(IQR), number (n) & percentage (%), Platelet-rich plasma(PRP), (T) t-test of significance, (C) Chi-Square test of significance, (F) Fisher's Exact test of significance, non-significant(NS), p<0.001** highly significant(HS).

change in AOFAS and percentage of change in diameter of fascia within the whole groups (r−0.661) and PRP group (r−0.682).

Therefore, a linear regression was conducted to examine how could percentage of change in diameter of fascia predict percentage of change in AOFAS at 6 weeks and 6 months within PRP group; for each one unit decrease in percentage of change in diameter of fascia, the percentage of change in AOFAS increased by 2.113 at 6 weeks. While for each one-unit decrease in percentage of change diameter of fascia, the percentage of change in AOFAS increased by 2.332 at 6 months (Figures 4,5).

Table 4. Diameter of fascia between the two studied groups.

			Drug used		Student t-test	
			PRP (*N*= 30)	Steroids (*N*= 30)	p-Value	Sig.
Diameter of fascia (mm)	Pre-injection	Mean ± SD	6.94 ± 0.81	6.89 ± 0.82	0.8	NS
	3w post-injection	Mean ± SD	6.48 ± 0.74	5.64 ± 0.63	<0.001**	HS
		% of change	−5.8%	−18.8%		
	6w post-injection	Mean ± SD	5.86 ± 0.68	5.74 ± 0.66	0.491	NS
		% of change	−14.5%	−17.4%		
	12w post-injection	Mean ± SD	5 ± 0.69	6.01 ± 0.55	<0.001**	HS
		% of change	−27.5%	−13.0%		
	6m post-injection	Mean ± SD	4.87 ± 0.71	6 ± 0.56	<0.001**	HS
		% of change	−29.0%	−13.0%		

Data were expressed as mean ± standard deviation (SD), median, interquartile range(IQR), number (n) & percentage (%), Platelet-rich plasma(PRP), weeks(w), months(m), (T) t-test of significance, (C) Chi-Square test of significance, (F) Fisher's Exact test of significance, non-significant(NS), p˂0.001** highly significant(HS). percentage(%), American orthopedic foot and ankle society(AOFAS), linear regression(R).

According to AOFAS grading, all patients were poor pre-injection, while at 6 weeks, PRP group had more fair 7 (23.33%) and good cases of 16 (53.33%) than steroids group [5 (16.67%), 13 (43.33%), respectively], without statistical significant difference. At 6 months follow-up, patients injected with PRP had statistically significant more good 6 (20%), and excellent grade 18 (60%) than steroids group [3 (10%), 0 (0%), respectively] (with p-Value was < 0.001).

As regarding the degree of patient satisfaction, there was significant increase in the PRP group being excellent in 18 patients (60%) of patients, good in 6 patients (20%), acceptable in one patient (3.3%) and poor in 5 patients (16.7%). While in steroid group, it was good in 3 patients (10%) of patients, acceptable in 16 patients (53.3%), poor in 11 patients (36.7%) with no patients of excellent degree.

Regarding need for analgesia along course of follow-up, there was significant increase in analgesic ingestion at 3 weeks post-injection in PRP group (with median 1.5 gm/day Vs 1 gm/day in steroid group). While at 12 weeks and 6 months, there was significant increase in analgesic ingestion in steroids group (with median 1.5 gm/day Vs 0.5 gm/day in PRP group), with non significant difference at 6 weeks (Figure 6).

4. Discussion

In this study, improvement in both clinically regarding VAS & AOFAS scores and radiologically regarding thickness and echogenicity of plantar fascia was observed in both PRP and the steroid groups, however steroid group showed early improvement with short duration

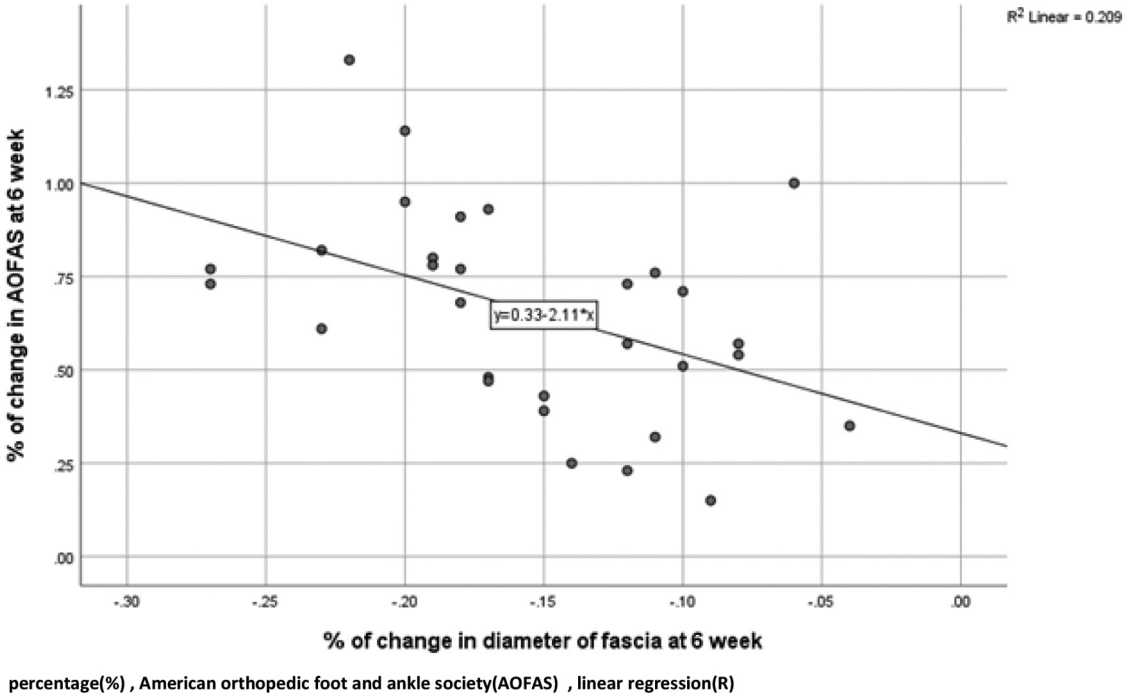
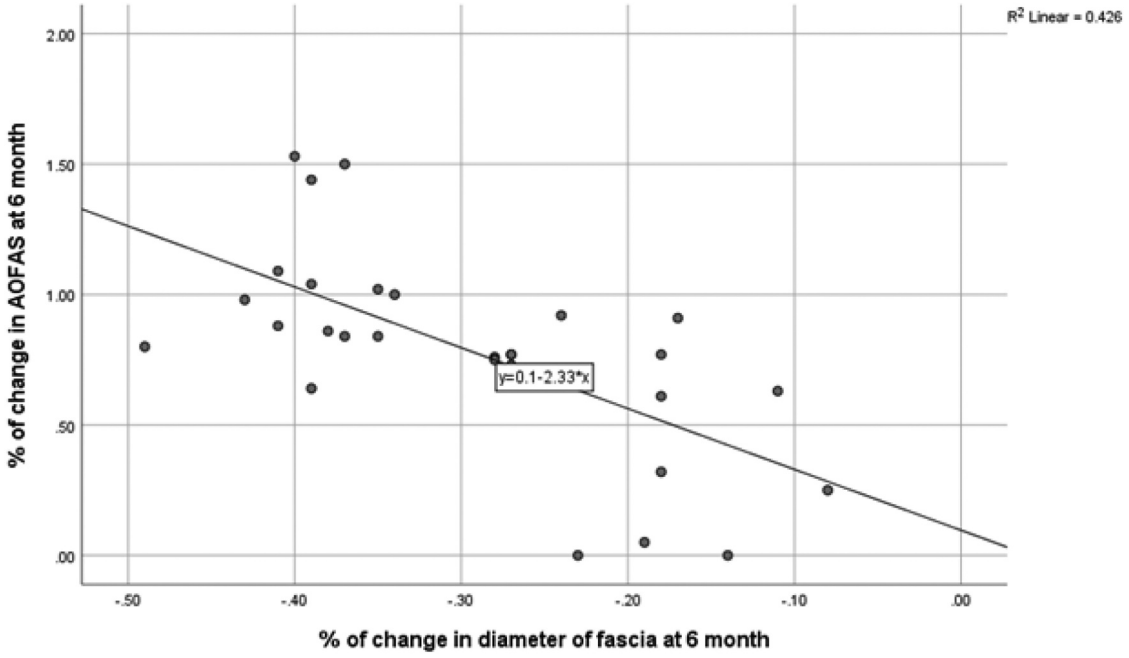
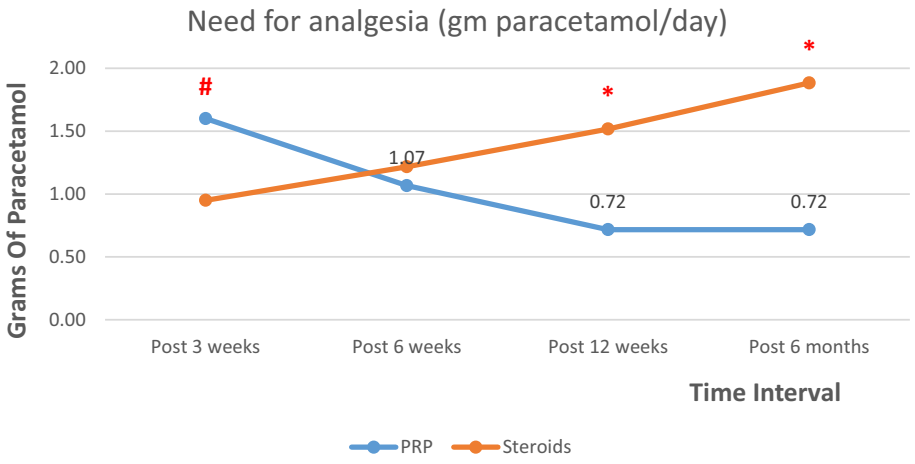


Figure 4. Correlation between percentage of change in AOFAS & diameter of fascia at 6 weeks. Percentage (%), American orthopedic foot and ankle society(AOFAS), linear regression(R)



Percentage (%) , American orthopedic foot and ankle society(AOFAS) , linear regression(R)

Figure 5. Correlation between percentage of change in AOFAS & diameter of fascia at 6 months.



Data were expressed as median, Platelet-rich plasma (PRP) , grams(gm) , weeks(w) , months(m) , * significant for PRP , # significant for steroids.

Figure 6. Need for analgesia along course of follow up.

while PRP group showed improvement 12 weeks post-injection till the end of the study (delayed onset but with long-duration improvement).

Plantar fasciitis is defined as localized inflammation and degeneration of the plantar aponeuroses [19]. Despite the diagnosis containing the segment "itis", **Becker and Childress** [20] found that the lack of inflammatory cells was a key feature of this disease.

The repetitive excessive loads on plantar fascia caused by long-distance running might cause fibrosis, degeneration, or even both. Mainly it is a degenerative irritation of the plantar fascia, which originates at the medial calcaneal tuberosity of the heel, and the nearby perifascial structures [19].

The results of the current study matched the results of **Tiwari** and **Bhargava** [21] who also compared the effect of PRP and steroid in treatment of plantar fasciitis on 60 patients. After 1, 3 and 6 months of treatment, VAS score significantly falls in both groups ($p < 0.001$), however, the decrease in VAS score was higher in PRP group more than steroid group.

Corticosteroid can accelerate the process of pain relief through its strong anti-inflammatory effect. Mechanism of action of injected corticosteroid, involves the inhibition of fibroblast proliferation and ground substance protein expression, which was observed in the pathological features of plantar fasciitis [22]. This explains rapid relief of pain &

improvement of function early after injection of steroids that reached its peak 3 weeks post-injection (pain reduction of 47.6%) and could be maintained up to 12 weeks.

According to a study by **Monto**, and **Raymond** [23], an increase in fascia thickness and a decrease in echogenicity of the plantar fascia can indicate the presence of edema and microtears in the fascia fibers. However, these effects were found to be reduced shortly after the administration of a steroid injection due to its anti-inflammatory properties, and the reduction in thickness and increase in echogenicity persisted for up to 6–12 weeks post-injection. It should be noted that the effects of steroid injection were found to be short-term and diminished over time.

All patients injected with PRP showed significant post-injection pain (for 72 hours) that needed analgesics in post-injection hours while no patients in steroid group showed post-injection pain (0%) that may be attributed to the following: in steroid group xylocaine 2% was mixed with methylprednisolone that was not performed in PRP group. In addition, it may be attributed to the process of healing in patients injected with PRP that can be summarized in the following three phases:

Phase1 (hemostasis and inflammation) is triggered by tissue injury and lasts for 2–5 days [24]. Degranulation of platelets occurs and the release of growth, bioactive, and hemostatic factors causing inflammation.

Phase 2: (proliferation) begins 2-days after injury and can last for 3 weeks [25].

Phase 3: (remodeling) follows and necessitates the maturation of collagen and the production of scar tissue and can take more than a year to complete.

This healing process may also explain the early significant difference in pain (high VAS) and the increase in diameter of plantar fascia in PRP group in comparison to steroid group 3 weeks post-injection that may be explained with inflammation during phase 1 and phase 2 induced by PRP injection. Then these parameters started to improve (VAS, thickness decreased & echogenicity increased) gradually after 6^{th} week due to remodeling that occurred in phase 3 with collagen maturation.

Similarly, the study of **Ragab and Othman** in **2012** demonstrated that, the thickness of plantar fascia dropped from 7.1 mm to 4.8 mm with PRP treatment ($p < 0.001$) after 10 months ultrasound follow-up of the plantar fascia thickness [26].

The results of the current study differed from the result of **Lee and Ahmad** [27] who also compared the effect of local injection of PRP and steroid in plantar fasciitis' treatment over a period of 6 months. They reported that corticosteroid was better regarding onset and, probably, extent of improvement. This difference may be attributed to that **Lee and Ahmed** injected 1.5 ml of autologous blood with 1 ml of Lignocaine 2% in PRP group while in steroid group, a mixture of 20 mg (0.5 ml of a 40 mg/ml solution) of Triamcinolone acetonide with 2 ml of Lignocaine 1% was injected (both blindly). However in the present study, 2.5 ml PRP was injected without mixing with local anesthetics as local anesthetics could directly interfere with the platelet functionality, especially platelet aggregation [28]. While, in the steroid group, a combination of 40 mg/ml of methylprednisolone and 1 ml of xylocaine 2% was applied (both guided with US).

A single-center study of 40 consecutive patients with refractory plantar fasciitis were chosen by **Jiménez-Pérez et al**. [29]. Although they used two local injections of 4 ml of PRP and 4 ml of 40 mg methylprednisolone in PRP and steroid group, respectively, they reported results that were similar to the results of the current study after 3 and 6 months follow-up. The clinical results of the PRP injection in their study were superior to steroids regarding VAS, AOFAS and the thickness of the fascia.

However, the previous study was neither a blinded nor a randomised study. Moreover, the method of production and the protocol of the PRP injections were not standardized and may not have been the best. In this regard, a number of commercially available technologies enable effective outpatient preparation.

In the present study, A 2.5 ml of PRP on sediment (platelet pellet) were obtained from 10 cc blood sample after two centrifugations, and suspend the platelet pellets by gently shaking the tube [14]. This volume was adequate with adequate concentration of platelets (2.5×10^6 platelets/2.5 mL) [30].

To determine the optimal concentration of platelets in PRP, previous studies have shown that endothelial cell proliferation peaks at 1.25×10^6 platelets/uL and angiogenesis at 1.5×10^6 platelets/uL [30]. These findings suggest that a platelet concentration of 1 million/uL is now widely considered to be the effective concentration for therapeutic PRP. However, administering excessive platelets could lead to negative effects such as apoptosis, receptor desensitization, and growth factor receptor down-regulation, resulting in paradoxical inhibition [31]. **Weibrich et al**. also demonstrated that highly concentrated platelets (6—11 ×; 1,845,000–3,200,000 platelets/uL) inhibited osteoblast activity compared to the more optimal lower concentrations. Therefore, injecting large volumes of highly concentrated platelets into the plantar fascia may cause fascia rupture [32].

In order to achieve the optimal response to PRP administration, it may be necessary to adjust the platelet concentration according to the type of tissue being treated. The varying levels of receptors in different tissues could explain why a specific concentration of PRP

has significant effects in one study involving a particular tissue type, but not in another study involving a different tissue. In a study by **Anitua et al**. [33], the effects of 2× and 4× PRP on tendon, dermal, and synovial fibroblasts were investigated. The results showed that different platelet concentrations had different positive effects on cell proliferation, hyaluronic acid production, and secretion of angiogenic growth factors. However, it was noted that the positive effects were not consistent across all tissue types, leading to the conclusion that the biological effects of growth factor-rich preparations may depend on both the concentration of platelets and the anatomical source of the cells [33].

Calcium chloride ($CaCl_2$) (50 µl of $CaCl_2$ in 1 ml of PRP) was added to PRP to activate growth factors, Calcium Chloride was added exogenously to PRP preparation resulting in the formation of a less condensed fibrin matrix. The fibrin matrix may provide a trapping mechanism for platelets resulting in smaller amounts of thrombin formation endogenously, allowing a slower release of growth factors over a 7-day period, which may enhance cell migration and healing [34].

Thickening of the plantar fascia is of particular interest, as it is a prominent and frequent manifestation of chronic plantar fasciitis and can be assessed quantitatively. Our results indicated that functional recovery (in terms of AOFAS scores) is not correlated with the degree of fascial thinning after Steroid treatment while it showed negative correlation in PRP group. **Ermutlu et al**. [35] that treated patients with betamethasone injection or extracorporeal shock wave therapy (ESWT) recorded no correlation between AOFAS scores and fascia thickness in both groups. In this study, authors used MRI in measuring plantar fascia thickness. Moreover, the negative correlation in the current study after injection of PRP may be consistent with the induced healing process by regeneration of plantar fascia that eliminate fibrous tissue and scar formation and so keeping elasticity of fascia and improving functional outcome.

Monto [36] concluded that PRP injection is more efficient (functional outcome AOFAS) with long duration than cortisone injection on long-run management (24 months) of severe chronic plantar fasciitis. A trial by **Shetty and his colleagues** [37] also compared PRP with corticosteroid, but they found no difference between the two. The drawback of Shetty and colleagues' study is the short follow-up of only 3 months.

None of our patients experienced any adverse effects after injection by the end of the study. No post-injection foot deformities nor infection were noted.

There remains a disagreement on which treatment modality is superior. Lack of a standardized study design, a variety of injectable forms and differences in assessment of outcomes make direct comparison of the studies difficult.

There were limitations in this study: our study was conducted based on relatively small sample size ($N < 100$). Smaller studies have a higher propensity to overestimate the therapeutic benefits when compared to bigger trials. Another limitation in our study was that patients' follow up was 6 months; with a longer follow-up time, we believe that it will have sufficient validity to accept its results and to detect which group will show sustained improvement and if relapses may occur in PRP group in the long-term follow-up.

5. Conclusion

Ultrasound-guided Injection of plantar fascia of 2.5 ml PRP has long-term improvement of pain, functional outcome and decreases fascial diameter and echogenicity with more patient satisfaction compared to 40 mg methylprednisolone acetate added to 1 ml lidocaine injection in patient with chronic plantar fasciitis. Thus, we recommend it as an alternative approach for patients with refractory plantar fasciitis.

Disclosure statement

No potential conflict of interest was reported by the authors.

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