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ORIGINAL ARTICLE

Local injection of autologous platelet rich plasma compared to corticosteroid treatment of chronic plantar fasciitis patients: A clinical and ultrasonographic follow-up study

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KEYWORDS

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Foot Health Status Questionnaire (FHSQ)

Abstract *Background:* Platelet-rich plasma (PRP) has been gaining popularity as a treatment for plantar fasciitis (PF).

Aim of the work: To compare local autologous PRP and steroid injections both clinically and sonographically within 3-months and also regarding its safety.

Patients and methods: This study was carried out on 50 patients with chronic PF divided into two groups: steroid and PRP groups ($n = 25$ each). Patients were assessed by visual analog scale (VAS), Foot Health Status Questionnaire (FHSQ) and ultrasonography at 1.5 and 3 months post-injection.

Results: The 50 patients had comparable disease duration ($p > 0.5$). At 1.5 months post-injection, there was more improvement in the PRP than in the steroid group both clinically (as assessed by the VAS) and ultrasonographically (as regards the echogenicity) ($p = 0.008$ and $p < 0.01$, respectively). There was no significant difference between both groups at 3 months. The echogenicity significantly improved at 3 months post-injection within each group ($p < 0.0001$). Regarding thickness, the difference did not reach significance ($p = 0.11$, $p > 0.05$). No significant difference was present between the 2 groups regarding the reduction plantar fascia thickness at 1.5 ($p = 0.89$) and 3 months ($p = 0.64$) post-injection. Regarding the safety of both injections, none of our patients in either group developed any significant complications.

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Conclusions: We suggest that the PRP injection is a new, readily available, well tolerated and safe choice of therapy for chronic PF and is not inferior to steroid injection in a short term 3 month follow up. Comparing the long-term efficacy both clinically and sonographically is necessary to confirm their sustained effect.

1. Introduction

Heel pain is a common presenting complaint in the foot and ankle practice. Plantar fasciitis (PF) is the most common cause of heel pain [1]. It tends to occur more often in women, middle-aged, military recruits, athletes and the obese [2]. Approximately 10% of people suffer from PF at some point during their lifetime [3].

Corticosteroid injections are used for cases of PF refractory to conservative treatment and have been an effective modality for pain relief [4]. However, the effect seems to be limited and short-lived [5]. Also, a number of complications may occur of which the most serious are plantar fascial rupture and plantar fat pad atrophy. Fascial rupture interrupts the intrinsic windlass mechanism of the foot and can promote further inflammation in the surrounding tissue. In addition, plantar fat pad atrophy diminishes subcalcaneal cushioning, availing the plantar fascia to further insult and, hence, more pain [6].

Platelet-rich plasma (PRP) has been gaining popularity as a treatment for PF. Injection of PRP is thought to be safe, and not to interfere with the biomechanical function of the foot [7]. It is a component of whole blood that is centrifuged to a concentrated state, treated with an activating agent, and injected into the affected area [8]. The basic biologic mechanism of action of PRP is simple, after injection of PRP in an injured area, it induces a local inflammation. The pro-inflammatory mediators together with the growth factors released from the granules of the platelets trigger the localized inflammation and the wound healing cascade, resulting in the cellular migration and proliferation, glycosaminoglycan and collagen deposition, collagen maturation and remodeling of the healing tissue at different stages of wound healing [9]. PRP therapy has been shown to improve pain scores and functional ability and to decrease plantar fascia thickness. In 2004, Barrett and Erredge treated nine patients with chronic PF with ultrasound-guided PRP injections. Seven patients reported complete resolution of symptoms and showed sonographic improvement [10]. Later on in 2011, Scioli performed PRP injections for PF and noted marked reduction in pain, and improved ability to stand and walk in nearly all his patients [11]. Similarly, Ragab and Othman in 2012 evaluated 25 patients and reported that VAS significantly improved and plantar fascia thickness dropped with PRP treatment [7].

There is still controversy regarding the effectiveness of PRP injections compared with steroid injections in PF patients. Omar et al. in 2012 carried out a randomized controlled trial on 30 patients and found a significant improvement in pain and foot function at 1.5 months after PRP compared to steroid injection [12]. More recently, Shetty et al. in 2014 found a better response with PRP injections at the end of a 3 month follow up [13]. Moreover, Monto found sustained improvement in the American Orthopedic Foot and Ankle Society (AOFAS) hind foot score at 3, 6, 12 and 24 months following PRP injection [14].

To date, all previous studies in this field have either assessed local autologous PRP injections alone clinically and sonographically, or compared PRP with steroid injections only clinically. The aim of this study was to compare local autologous PRP injections and local steroid injections both clinically and sonographically within 3 months regarding its effect on pain, function, thickness and echogenicity of the plantar fascia and also regarding its safety.

2. Patients and methods

2.1. Patients

This study was carried out as a prospective, single-center, randomized, blind comparative study on 50 patients with chronic PF, attending the Rheumatology and Rehabilitation outpatient clinic in Zagazig University Hospitals, Faculty of Medicine. An approval had been obtained from the Institutional Review Board (IRB) of Zagazig University and all participants signed an informed consent.

Patients were included in the study if they were >18 years old and had chronic PF (>3 months). Clinical diagnosis of the patients was considered in those having inferior heel pain that usually worsens with their first steps in the morning or after a period of inactivity, with maximal tenderness over the anteromedial aspect of the inferior heel. The diagnosis was also confirmed by ultrasonography based on having plantar fascia thickness greater than 4 mm.

Patients were excluded if they had bilateral PF (for sonographic comparisons), received non-steroidal anti-inflammatory drugs (NSAIDs) within 1 week before the study, had a previous local injection or surgery for PF, had haematological disorder like anemia (hemoglobin $<$ 7.0 g/dl), thrombocytopenia (platelets $<$ 15,000/μL) or bleeding dyscrasias, had associated inflammatory enthesitis such as spondyloarthropathies, cardiovascular, renal or hepatic disease, bacteremia, cellulitis, skin ulceration, vascular insufficiency or neuropathy related to heel, diabetes mellitus or allergy to bupivicaine. Pregnant and breast feeding patients were also excluded.

The chronic PF patients were allocated randomly using a simple randomization method (odd for PRP and even for steroid) into two equal groups (25 patients each) by one of the researchers who injected the patients with either steroids or PRP (not guided by ultrasound) and did not share in clinical nor in ultrasonographic assessments: Group I (PRP) was injected 3 ml PRP after local anesthetic injection [15] and group II (steroid) was injected 2 ml triamcinolone acetonide (40 mg/ml) with local anesthesia [16]. The clinical examiners and sonographers were blind to the type of the given injection.

2.2. Clinical and ultrasonographic assessment

Pre-injection all patients of our study were subjected to full history taking, thorough physical examination, visual analog scale (VAS: 0–100) [17], Foot Health Status Questionnaire (FHSQ) which includes Short Form 36 (SF36) [18], complete blood count (CBC) to exclude anemia and thrombocytopenia, plain X-ray to detect calcaneal spur, and ultrasonography. Patients were reassessed by VAS, FHSQ, and ultrasonography at 1.5 and 3 months post-injection.

Sonographic examination was performed with 5–12 MHZ linear array transducer (Medison R3) on both symptomatic and asymptomatic heels. The patients lay prone and their ankles dorsiflexed to 90°. The thickness of the plantar fascia was measured on the longitudinal view of the heel from the anterior edge of the inferior calcaneal border. PF was defined as plantar fascia thickness >4 mm or when there was >1 mm difference in plantar fascia thickness between symptomatic and asymptomatic heels in association of reduced echogenicity and/or loss of definition of border of the fascia distal to the antero-inferior border of the calcaneus [19].

Ultrasonographic examination was repeated in the same visit by another sonographer to assess inter-readers' reliability. No significant difference was found between the two readers as regards the plantar fascia thickness ($t = 0.045$, $p = 0.9$, $p > 0.05$), and echogenicity (kappa agreement was 0.71 (good)) and was highly significant ($p = 0.003$, $p < 0.01$).

2.3. Preparation of PRP

It began with a venous puncture and subsequent collection of specific volume of autologous blood from the patient (10-ml of venous blood sample) [20] into a tube containing an anticoagulant (sterile sodium citrated tubes). The tubes were centrifuged at 1800 rotations/minute (rpm) (for 15 min) separating plasma (top layer) from packed red blood cells (RBCs) (bottom layer). The RBC layer is discarded and the second centrifuge at 3500 rpm for 10 min yields a more concentrated platelet layer after extraction of platelet poor plasma. Platelets rich in growth factors were obtained following Anitua's technique that recommends removal of leukocytes because their presence has been associated with the release of metalloproteases that could damage the tissues and prevent tissue healing [21].

2.4. Injection technique

Patients lay in supine position. Skin of the heel was disinfected by betadine. For the PRP group, after injecting 1-ml of local anesthesia (mepivacaine) PRP was injected by the same syringe in the tenderest area [15]. As soon as the needle was out, we placed a bandage over the injected area. The patient was observed for 10 min and then discharged. The same steps were followed for the steroid group of patients except that 2 ml triamcinolone acetonide (40 mg/ml) was injected with local anesthesia [16]. After the procedure, patients were not allowed to bear weight for 3 days. They were advised to wear comfortable shoes, and avoid running and other high impact activities for 10 days. A standard stretching program for plantar fascia was given to all patients [15].

As PRP effectively induces an inflammatory response, some patients experienced minimal to moderate discomfort following the injection which may last for up to 1 week. They were instructed to ice the injected area if needed for pain control and modify activity as tolerated. We recommended acetaminophen as the optimal analgesic, and avoided use of NSAID's throughout our 3 month follow up period as they exhibit anti-platelet and anti-coagulant effects, which may diminish the effectiveness of PRP [22].

2.5. Statistical analysis

Data were analyzed by the Statistical Package for the Social Sciences (SPSS) software version 20.0. Differences between qualitative variables were compared by Chi-square test (χ^2) and differences between quantitative variables in two groups were compared by Student's t test (parametric) and by Mann–Whitney U test (non-parametric). Multiple quantitative data were compared by ANOVA test (parametric) and by Kruskal–Wallis test (non-parametric). Kappa agreement was used to test agreement between findings of the two sonographers. Significance was considered at p-value <0.05.

3. Results

There was no significant difference between the two groups regarding age (PRP group: 37.48 ± 8.75 years, steroid group: 38.52 ± 6.2 years) and sex (PRP group: F:M = 23:2, steroid group: F:M = 25:0) ($p > 0.05$). Disease duration in the PRP

Table 1 Comparison between the platelet-rich plasma (PRP) and steroid groups regarding visual analog scale (VAS) and short form (SF36) in chronic plantar fasciitis patients, pre-injection, at 1.5 and 3 months post-injection.

Parameter	PRP group ($n = 25$)	Steroid group ($n = 25$)	t	p
VAS, median (range)				
Pre-injection	9 (8–10)	10 (9–10)	−1.7	0.07
At 1.5 mo	1.5 (0–10)	4 (0–9)	−2.6	0.008
At 3 mo	0 (0–10)*	1 (0–9)*	−1.1	0.24
SF 36, mean ± SD				
Pre-injection	173.4 ± 16.2	171.2 ± 11.5	0.55	0.58
At 1.5 mo	232.8 ± 64.1	225.2 ± 38.9	0.51	0.62
At 3 mo	246 ± 66.7*	249 ± 73.22*	−0.15	0.88

PRP: Platelet-rich plasma, VAS: visual analog scale, SF36: Short Form 36.
* Significantly different from the corresponding value pre-injection ($p < 0.001$).

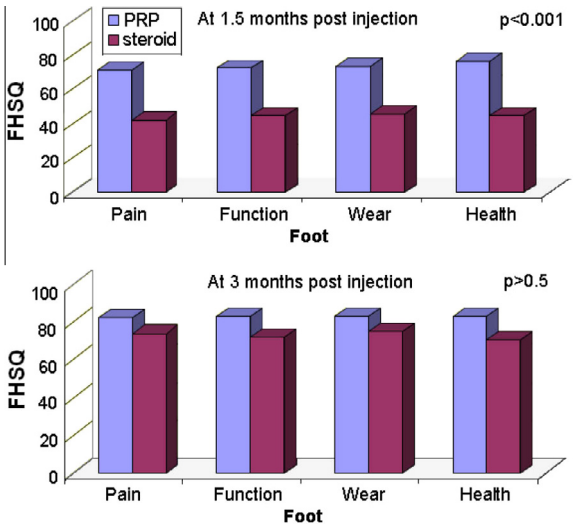

Figure 1 Comparison between the platelet-rich plasma (PRP) and steroid injection groups of patients with chronic plantar fasciitis as regards the Foot Health Status Questionnaire (FHSQ) foot domains at 1.5 months post-injection (Upper bar chart) (t = 3.51, 3.41, 3.45 and 4.05 for foot pain, function, wear and health respectively; $p < 0.001$ each) and at 3 months post-injection (t = 0.88, 1.11, 0.86 and 1.31 respectively; $p > 0.05$).

group was 7.25 ± 1.12 months and in the steroid group it was 7.58 ± 1.02 months and the difference was also insignificant ($p > 0.05$). Calcaneal spur was found in only 4 patients of the PRP group and in 14 of the steroid group. Table 1 shows the VAS and SF36 in the two groups pre-injection, 1.5 months and 3 months post-injection. At 1.5 months post-injection there was a significant difference between both groups regarding VAS ($p < 0.01$). The difference between pre-injection and 3 months post-injection FHSQ within each group was highly significant ($p < 0.001$). Fig. 1 shows the FHSQ in both groups at 1.5 and 3 months post-injection. There was a significant improvement in the FHSQ at 1.5 months post-injection in the PRP group compared to the steroids group ($p < 0.001$).

Table 2 and Figs. 2 and 3 show the sonographic findings (plantar fascia thickness and echogenicity) in the two groups pre-injection, 1.5 and 3 months post-injection. The echogenicity significantly improved at 3 months post-injection within each group ($p < 0.0001$). Regarding thickness, the difference did not reach significance ($p = 0.11$, $p > 0.05$). No significant difference was present between the 2 groups regarding the reduction plantar fascia thickness at 1.5 ($p = 0.89$) and 3 months ($p = 0.64$) post-injection. A significant improvement in echogenicity was present at 1.5 months between the two groups favoring the PRP group ($p < 0.01$). At 3 months post-injection no significant difference was observed between both groups as more patients from the steroid group became normoechoic ($p = 0.7$). Regarding the safety of both injections, none of our patients in either group developed any significant complications.

4. Discussion

Plantar fasciitis is the most common cause of heel pain [1] and injury of the plantar fascia [23]. Our study was designed to compare the effect of autologous PRP injection with the classic steroid injection in treatment of chronic PF both clinically and sonographically within 3 months, noticing its short-term efficacy and safety.

Our results showed that both groups showed significant clinical and sonographic improvement at the end of the 3 months follow up period without any complications. More improvement, both clinical and sonographic, was observed in the PRP than in the steroid group at 1.5 months post-injection. The early improvement with PRP is most probably mediated by the excessive amount of growth factors and cytokines that creates an inflammatory response that subsequently restarts the cycle of tendon repair interrupting the stagnant healing environment [24]. While with steroid injections it only serves as an anti-inflammatory agent that ceases the inflammation early within days and has a negligible effect on regeneration, remodeling and maturation phase [25] which occurs at a much slower rate compared with the PRP environment rich in growth factors.

Table 2 Comparison between the platelet-rich plasma (PRP) and steroid groups regarding the sonographic findings in chronic plantar fasciitis patients, pre-injection, at 1.5 and 3 months post-injection.

Parameter	PRP group (n = 25)	Steroid group (n = 25)	t	p
Thickness				
Pre-injection	6.18 ± 1.51	5.67 ± 0.73	0.62	0.54
At 1.5 mo	5.68 ± 1.65	5.45 ± 0.77	0.14	0.89
At 3 mo	5.19 ± 1.66	5.14 ± 0.65	−0.47	0.64
Echogenicity			χ^2	p
Pre-injection				
Normoehoic	0 (0)	0 (0)	0	1
Hypoechoic	25 (100)	25 (100)		
At 1.5 mo				
Normoechoic	20 (83.3)*	9 (36)	11.3	< 0.01
Hypoechoic	4 (16.7)	16 (64)		
At 3 mo				
Normoechoic	20 (83.3)	19 (79.2)*	0.13	0.7
Hypoechoic	4 (16.7)	5 (20.8)		

PRP: Platelet-rich plasma.
* = Significantly different from the corresponding value pre-injection ($p < 0.0001$).

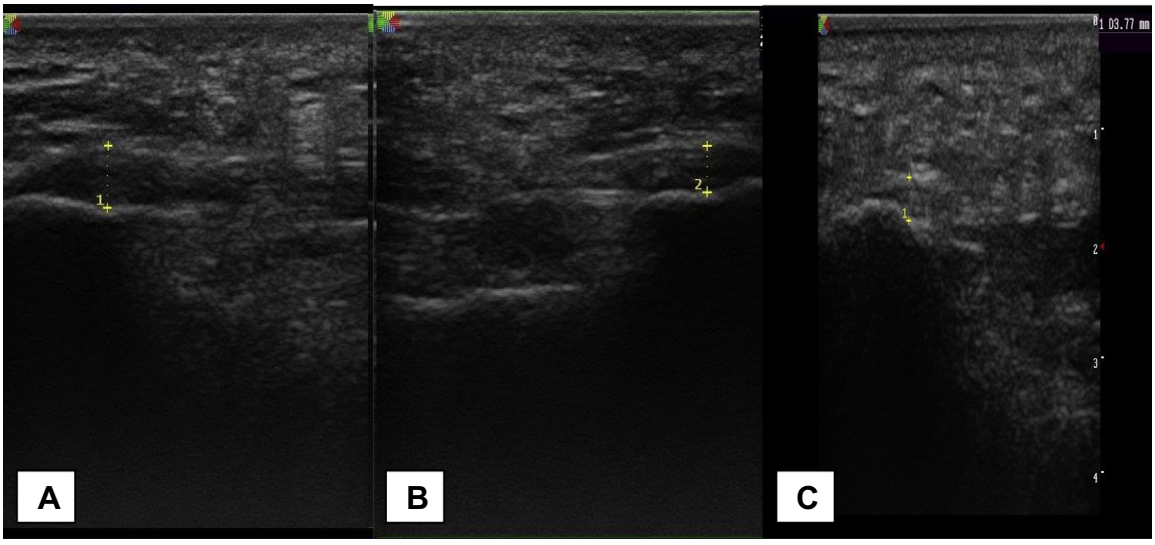

Figure 2 Sonographic changes in PRP group. A: (before injection) plantar fascia thickness was 6.58 mm and fascia is hypoechoic. B: (after 45 days) thickness was 4.81 mm and echogenicity was better. C: (after 3 months) thickness was 3.77 mm and fascia became hyperechoic.

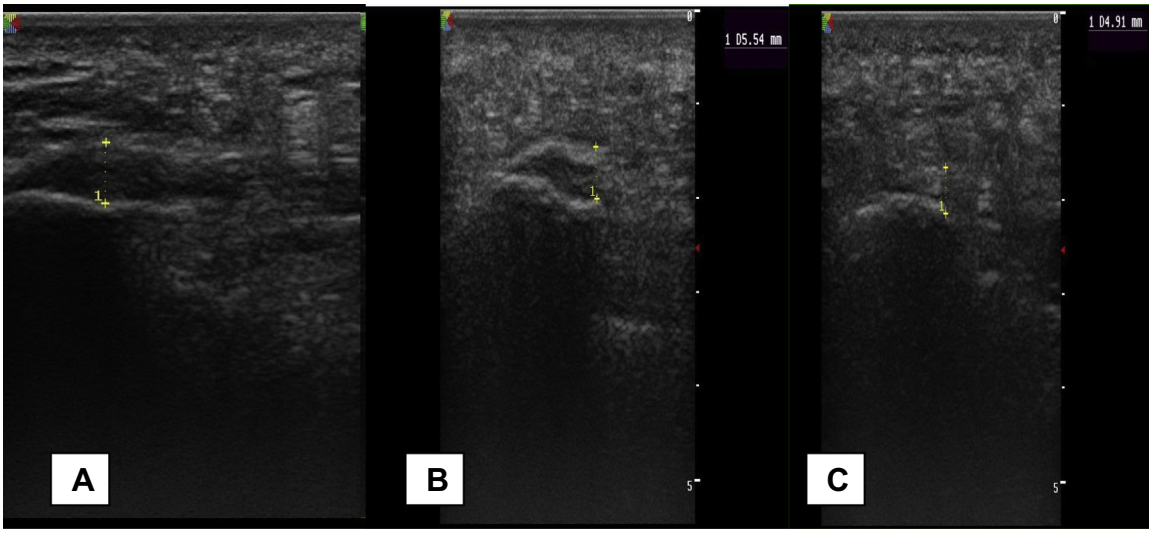

Figure 3 Sonographic changes in steroid group. A: (before injection) plantar fascia thickness was 6.58 mm and fascia was hypoechoic. B: (after 45 days) thickness was 5.54 mm and fascia was still hypoechoic. C: (after 3 months) thickness was 4.91 mm and fascia became hyperechoic.

At the completion of the study at 3 months, neither the PRP group nor the steroid group proved to have better improvement regarding clinical parameters. Also sonographically, although the reduction in plantar fascia thickness remained insignificant between the two groups throughout the 3 months, the percentage of normoechoic patients in the PRP group remained constant while more patients in the steroid group became normoechoic making the difference between them which was significant at 1.5 months insignificant at 3 months. This is probably due to the slower healing in the steroid injection group which finally became comparable to the PRP group at 3 months.

The results of our study showing a good response to PRP injections at the end of 3 months follow up was supported by several previous studies on PRP in chronic PF [7,10,11]. It was also consistent with another study on PRP injection in patients with chronic tendinopathy/fasciopathy in the upper and lower limbs as 84% of patients had an improvement in echo texture whereas the reduction in maximal thickness did not reach statistical significance ($p < 0.09$) [26]. On the other hand in 2013, the Cochrane database review on eight different soft tissue injuries concluded that overall, there is still insufficient evidence to support the use of PRP for treating musculoskeletal soft tissue injuries, but it considered the need for future randomized controlled trials on specific clinical conditions rather than multiple different conditions and the need for standardization of PRP preparation methods [27].

Our PRP versus steroid comparison matched the results of recent studies as that of Omar et al. who found a significant difference as regards VAS and FHSQ between the two groups

favoring the PRP group at 1.5 months follow up ($p < 0.05$) [12] and also that of Monto who demonstrated that both PRP and steroid groups continued to improve up to 3 months and found that the improvement in the steroid group started to decline after 3 months and was sustained for longer periods in the PRP group [13].

In the current study, only four patients had a calcaneal spur on radiography in the PRP group showing no improvement neither clinically nor radiologically while patients with spurs in the steroid group showed improvement. The randomized selection of patients is thus a limitation of this study. A longitudinal larger scale study is required as further follow up beyond three months could help in detecting which group will show sustained clinical and sonographic improvement on a long-term follow up.

To the best of our knowledge this is the first study to compare PRP and steroid injections for chronic PF both clinically and sonographically. It could be concluded that although the cost of a PRP injection is higher than a steroid injection, PRP injections can still be considered a readily available, well tolerated and safe choice of therapy for chronic PF. The efficacy of PRP injections in treating PF was found to be comparable to steroid injections in short-term follow up with earlier initiation of healing. Comparing the efficacy of PRP and steroid injections both clinically and sonographically in long-term follow up is necessary to see which will have a sustained effect beyond 3 months since all previous studies were based on clinical assessments only.

Conflict of interest

None.

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