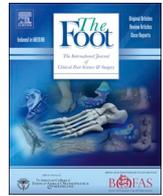




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Original Article

Similar effect of ultrasound-guided platelet-rich plasma versus platelet-poor plasma injections for chronic plantar fasciitis

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ABSTRACT

Background: There are conflicting reports regarding the therapeutic effect of platelet-rich plasma (PRP) versus autologous whole-blood (platelet poor plasma, PPP) injections for plantar fasciitis. Therefore, this study was conducted to compare the effectiveness of a single ultrasound (US)-guided PRP versus PPP injection in patients with chronic plantar fasciitis.

Materials and methods: 36 patients were recruited with clinical and sonographic evidence of chronic (>6 months) plantar fasciitis, refractory to analgesics and physical therapy in a double-blinded, randomized, prospective study. The patients were randomly allocated into two groups with a sealed envelope method. Group A included 18 patients who underwent a single US-guided PRP injection and group B included another 18 patients who underwent PPP injection with the same technique. Follow-up was set at 3 and 6 months; no patient was lost to follow-up. Pain, function and satisfaction were assessed using visual analogue scales, and occurrence of complications.

Results: All scores statistically significantly improved for both groups from baseline at the 3- and 6-month follow-up evaluation, without, however, any statistically significant differences between the two groups with respect to pain, function and satisfaction scores. Complications were not observed.

Conclusions: A single US-guided PRP injection yields similar results with PPP injection in patients with chronic plantar fasciitis. Both treatments provide significant improvement at 3 and 6-month follow-up after the injection.

1. Introduction

Previous studies reported on the favorable therapeutic effect of platelet-rich plasma (PRP) for various musculoskeletal injuries [1–3]. However, there is insufficient evidence to support the standardized clinical use of PRP for these injuries [4], and high-quality clinical data for standardized protocols and treatment recommendations are missing [5]. Recently, there has been growing interest in PRP injections for chronic plantar fasciitis [6–9], however, through a limited number of controlled trials [7]. Wilson et al. showed that PRP is a safe therapeutic option with the ability to decrease heel pain in patients with chronic plantar fasciitis refractory to appropriate conservative management [8]. Other authors reported that PRP injections are associated with improved pain and function when compared with corticosteroid injections in these patients [9]. However, other studies did not confirm these reports [10–12]. A prospective comparative clinical trial reported

similar effectiveness between PRP and autologous whole blood for the treatment of chronic plantar fasciitis in short-term [11], and a systematic review concluded that no clear indications for using PRP in the foot and ankle [12].

To clarify these conflicting reports, this study was conducted to compare the effectiveness of a single ultrasound (US)-guided PRP versus PPP injection for patients with chronic plantar fasciitis. The null hypothesis was that PRP yields no difference than PPP for this entity.

2. Materials and methods

A prospective, double-blind, randomized, single-center study in patients with chronic plantar fasciitis that was refractory to appropriate treatments for a minimum of 6 months was conducted. There were 36 patients diagnosed and treated from October 2013 to October 2015. Inclusion criteria were patients older than 18 years, US diagnosed

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plantar fasciitis and persistent clinical symptoms not responding to analgesics, non-steroidal anti-inflammatory drugs, physical therapy, stretching and ice therapy for 6 months. Exclusion criteria were patients with rheumatologic diseases, known malignancy, bleeding disorders, previous local surgery, extracorporeal shock wave therapy on the foot and ankle, and regional osteoarthritis; pregnant women, patients with peripheral neuropathies of the foot, and those who had undergone a local corticosteroid injection in the affected heel within the previous 3 months were also excluded. The patients were studied at 3 and 6 months; no patient was lost to follow-up. All patients gave written informed consent for their data to be included in this study. This study was approved by the Institutional Review Board of the authors' institution.

The patients were randomly allocated into 2 groups using a sealed envelope method of randomization. Group A included 18 patients who underwent a single US-guided PRP injection at the proximal insertion of the plantar aponeurosis, and group B included another 18 patients who underwent PPP injection using the same technique. The injection was done under sterile conditions with skin antisepsis, coverage of the ultrasound probe with a sterile pad, and use of the appropriate gel by the same physician who simultaneously managed the ultrasound device (free hand one man's technique by a single doctor who holds the syringe with one hand and scans with the probe with his other hand). Before the injection, subcutaneous local anaesthetic infiltration with 4 ml lidocaine solution was done in all patients. The physician who performed the injection was blinded to the type of injection that was administered. Under continuous US imaging, the tip of the needle was inserted into the proximal insertion of the plantar fascia and injection of the PRP or PPP was done. After 3 days rest, all patients were encouraged to resume normal daily and occupational activities without any other treatment thereafter.

The patients were evaluated at the baseline and at the 3 and 6-month follow-up by independent physicians who were blinded to which type of injection the patients had. Pain, function and satisfaction from the end-result of the procedure were evaluated using a 0–100 points visual analogue scale (VAS) with 0 point referring to no pain, worse function and satisfaction, and 100 points referring to worse pain, excellent function and satisfaction. Complications related to the procedure were recorded.

A power analysis (G-power computer software) was done to determine the sample size and the power of the study. Power analysis has shown that 18 patients were needed for each group of patients to produce a study with 80% power and 5% significance. The t-test and chi square test was employed in order to statistically analyze our findings. All reported p values were based on two-sided tests and compared to a significance level of 5%. Continuous variables are presented as means and Standard Deviations (SD). Categorical variables are expressed as absolute and relative frequencies (%). At baseline, statistical analysis showed no differences between the study groups with respect to age, pain, function and satisfaction (statistical criterion, t-test), gender, right or left foot (statistical criterion, chi square). The rate of success was calculated per group by the number of patients who were found with an individual VAS score of 0–20 points at their final follow-up; these patients were considered to have healed [13].

3. Results

All scores statistically significantly improved for both groups at the 3- and 6-month follow-up evaluation, however, without any statistically significant differences (t-test) between the two groups with respect to VAS-pain, VAS-function and VAS-satisfaction scores. Complications related to the procedure were not observed in either group. More specifically,

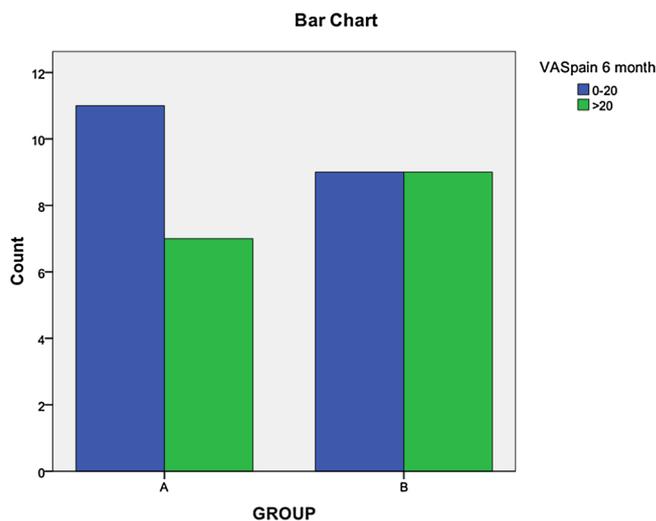


Fig. 1. VAS-pain scores were not different between group A and group B from baseline to the 3-month ($p = 0.702$) and the 6-month follow-up ($p = 0.250$).

3.1. Pain

The mean VAS-pain scores were not statistically significant different between the two groups at the 3-month ($p = 0.702$) and the 6-month follow-up ($p = 0.250$) (Fig. 1). Group A patients statistically significantly improved from baseline (74 ± 17.9 points) to the 3-month (42 ± 29.2 points; $p = 0.001$) and the 6 month follow-up (29 ± 34.4 points; $p < 0.001$). Improvement was also statistically significant between the 3 and 6-month follow-up ($p = 0.015$). Group B patients statistically significantly improved from baseline (69 ± 19.7 points) to the 3-month (38 ± 31.7 points; $p < 0.001$) and the 6 month follow-up (43 ± 37 points; $p < 0.001$). Improvement was statistically significant at the 3-month follow-up ($p < 0.001$) but not at the 6-month follow-up ($p = 0.356$).

3.2. Function

The mean VAS-function scores were not statistically significant different between the two groups at the 3-month ($p = 0.879$) and the 6-month follow-up ($p = 0.624$) (Fig. 2). Group A patients statistically significantly improved from baseline (17 ± 15.6 points) to the 3-month (58 ± 32.5 points; $p = 0.001$) and the 6-month follow-up (46 ± 41.7 points; $p = 0.026$). Improvement was not statistically significant between the 3 and 6-month follow-up ($p = 0.081$). Group B patients statistically significantly improved from baseline (23 ± 19.1 points) to the 3-month (56 ± 32.6 points; $p < 0.001$) and the 6-month follow-up (40 ± 39.1 points; $p = 0.013$). Improvement was also statistically significant between the 3 and 6-month follow-up ($p = 0.007$).

3.3. Satisfaction

The mean VAS-satisfaction scores were not statistically significant different between the two groups at the 3-month ($p = 0.686$) and the 6-month follow-up ($p = 0.669$) (Fig. 3). Group A patients statistically significantly improved from baseline (18 ± 19.4 points) to the 3-month (66 ± 34.8 points; $p < 0.001$) and the 6-month follow-up (73 ± 36.1 points; $p < 0.001$). Improvement was not statistically significant between the 3 and 6-month follow-up ($p = 0.055$). Group B patients statistically significantly improved from baseline (21 ± 20 points) to the 3-month (70 ± 30.5 points; $p < 0.001$) and the 6-month follow-up (68 ± 33.4 points; $p < 0.001$). Improvement was not statistically significant between the 3 and 6-month follow-up ($p = 0.063$).

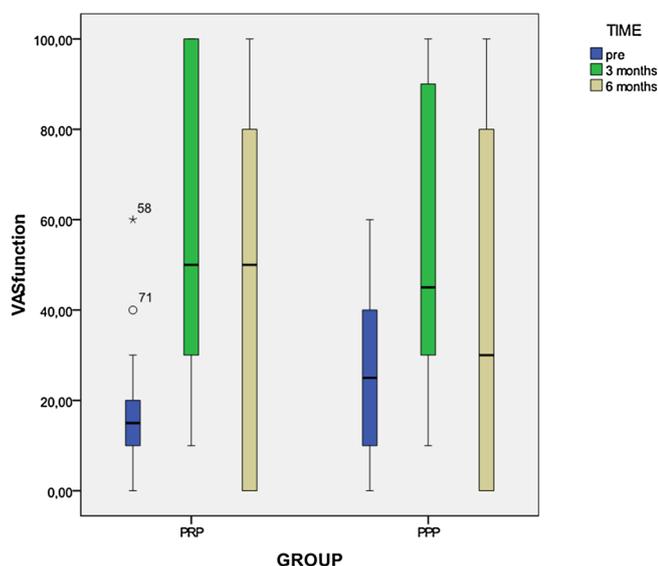


Fig. 2. VAS-function scores were not different between group A and group B from baseline to the 3-month ($p = 0.879$) and the 6-month follow-up ($p = 0.624$).

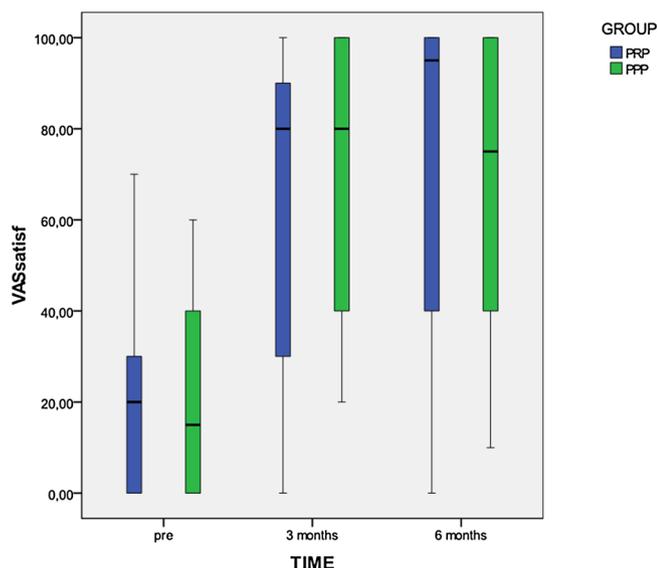


Fig. 3. VAS-satisfis scores were not different between group A and group B from baseline to the 3-month ($p = 0.686$) and the 6-month follow-up ($p = 0.669$).

4. Discussion

Plantar fasciitis is considered a degenerative tissue condition rather than original inflammation at the origin of the plantar fascia at the tuberosity of the calcaneus [14]. The plantar fascia is inaccessible to high concentrations of platelets and growth factors because of hypovascularity and hypocellularity; however, PRP injections may enable delivery directly to the lesion site [15,16]. In the present study, PRP injections was hypothesized to yield no difference to PPP injections with respect to pain, function and satisfaction of the patients with chronic plantar fasciitis. The results showed similar effect; these results confirmed the null hypothesis of our study. Therefore, PRP injections should not be recommended over autologous total blood injections as an optimal treatment option for these patients. Furthermore, the findings from the present study raise concerns regarding the superiority of PRP over PPP for similar musculoskeletal entities [17–23].

The rationale for using PRP is to increase tendon regenerative

abilities with a high content of cytokines and cells in hyperphysiologic doses, which should promote cellular chemotaxis, matrix synthesis, and proliferation [16]. However, despite that, there is strong evidence indicating that PRP or PPP injections do not improve plantar fasciitis-related pain or function when compared with other conservative methods [17]. Recently, an *in vivo* study showed surprisingly that PPP had an earlier angiogenic effect when compared with PRP [18]. Various experimental studies in different musculoskeletal areas have shown that PPP injections have similar biological responses with PRP and may exert a positive effect on degenerative or wound tissue remodeling [19–23]. To the best of the authors' knowledge, the present study is the first clinical trial to compare the clinical and functional outcomes of PRP and PPP for patients suffering from chronic persistent plantar fasciitis. Up to the 6-month follow-up after the injection, our results showed that both treatment options were similarly effective for these patients. Although there were no significant differences regarding the final pain, function and satisfaction scores between the two study groups, we noticed a trend in favour of the PRP group as for the final pain improvement; still, however, this difference was not statistically important.

In conclusion, a single US-guided PRP injection yields similar results with PPP injection in patients with chronic plantar fasciitis. Both treatments provide significant improvement at 6-month follow-up after the injection. This finding questions the superiority of the PRP injection for these patients. Further studies with longer term follow-up would be welcomed.

Conflict of interest statement

None. No benefits have been or will be received from a commercial party related directed or indirectly to the subject matter of this article.

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References

- [1] Majewski M, Ochsner PE, Liu F, Fluckiger R, Evans CH. Accelerated healing of the rat Achilles tendon in response to autologous conditioned serum. *Am J Sports Med* 2009;37:2117–25.
- [2] McCarrel T, Fortier L. Temporal growth factor release from platelet-rich plasma, trehalose lyophilized platelets, and bone marrow aspirate and their effect on tendon and ligament gene expression. *J Orthop Res* 2009;27:1033–42.
- [3] Schnabel LV, Mohammed HO, Miller BJ, McDermott WG, Jacobson MS, Santangelo KS, et al. Platelet rich plasma (PRP) enhances anabolic gene expression patterns in flexor digitorum superficialis tendons. *J Orthop Res* 2007;25:230–40.
- [4] Grambart ST. Sports medicine and platelet-rich plasma: nonsurgical therapy. *Clin Podiatr Med Surg* 2015;32(1):99–107.
- [5] Andia I, Maffulli N. Muscle and tendon injuries: the role of biological interventions to promote and assist healing and recovery. *Arthroscopy* 2015;31(5):999–1015.
- [6] Franceschi F, Papalia R, Franceschetti E, Paciotti M, Maffulli N, Denaro V. Platelet-rich plasma injections for chronic plantar fasciopathy: a systematic review. *Br Med Bull* 2014;112(1):83–95.
- [7] Hsiao MY, Hung CY, Chang KV, Chien KL, Tu YK, Wang TG. Comparative effectiveness of autologous blood-derived products, shock-wave therapy and corticosteroids for treatment of plantar fasciitis: a network meta-analysis. *Rheumatology (Oxford)* 2015;54(9):1735–43.
- [8] Wilson JJ, Lee KS, Miller AT, Wang S. Platelet-rich plasma for the treatment of chronic plantar fasciopathy in adults: a case series. *Foot Ankle Spec* 2014;7(1):61–7.
- [9] Singh P, Madanipour S, Bhamra JS, Gill I. A systematic review and meta-analysis of platelet-rich plasma versus corticosteroid injections for plantar fasciopathy. *Int Orthop* 2017;41(6):1169–81.
- [10] Yang WY, Han YH, Cao XW, Pan JK, Zeng LF, Lin JT, et al. Platelet-rich plasma as a treatment for plantar fasciitis: A meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2017;96(44):e8475.
- [11] Vahdatpour B, Kianimehr L, Ahrar MH. Autologous platelet-rich plasma compared with whole blood for the treatment of chronic plantar fasciitis: a comparative clinical trial. *Adv Biomed Res* 2016;5:84.
- [12] Vannini F, Di Matteo B, Filardo G, Kon E, Marcacci M, Giannini S. Platelet-rich plasma for foot and ankle pathologies: a systematic review. *Foot Ankle Surg* 2014;20(1):2–9.
- [13] Grecco MV, Brech GC, Greve JM. One-year treatment follow-up of plantar fasciitis:

- radial shockwaves vs. conventional physiotherapy. *Clinics (Sao Paulo)* 2013;68(8):1089–95.
- [14] Lemont H, Ammirati KM, Usen N. Plantar fasciitis: a degenerative process (fasciosis) without inflammation. *J Am Podiatr Med Assoc* 2003;93:234–7.
- [15] Fenwick SA, Hazleman BL, Riley GP. The vasculature and its role in the damaged and healing tendon. *Arthritis Res* 2002;4:252–60.
- [16] Marx RE. Platelet-rich plasma: evidence to support its use. *J Oral Maxillofac Surg* 2004;62:489–96.
- [17] Sandrey MA. Autologous growth factor injections in chronic tendinopathy. *J Athl Train* 2014;49(3):428–30.
- [18] Shahidi M, Vatanmakanian M, Arami MK, Sadeghi Shirazi F, Esmaeili N, Hydarporian S, et al. A comparative study between platelet-rich plasma and platelet-poor plasma effects on angiogenesis. *Med Mol Morphol* 2018;51(1):21–31.
- [19] Yilmaz S, Kabadayi C, Ipci SD, Cakar G, Kuru B. Treatment of intrabony periodontal defects with platelet-rich plasma versus platelet-poor plasma combined with a bovine-derived xenograft: a controlled clinical trial. *J Periodontol* 2011;82(6):837–44.
- [20] Miroshnychenko O, Chang WT, Drago J. The use of platelet-rich and platelet-poor plasma to enhance differentiation of skeletal myoblasts: implications for the use of autologous blood products for muscle regeneration. *Am J Sports Med* 2017;45(4):945–53.
- [21] Hatakeyama I, Marukawa E, Takahashi Y, Omura K. Effects of platelet-poor plasma, platelet-rich plasma, and platelet-rich fibrin on healing of extraction sockets with buccal dehiscence in dogs. *Tissue Eng A* 2014;20(3–4):874–82.
- [22] Cáceres M, Martínez C, Martínez J, Smith PC. Effects of platelet-rich and -poor plasma on the reparative response of gingival fibroblasts. *Clin Oral Implants Res* 2012;23(9):1104–11.
- [23] Martínez CE, González SA, Palma V, Smith PC. Platelet-poor and platelet-rich plasma stimulate bone lineage differentiation in periodontal ligament stem cells. *J Periodontol* 2016;87(2):e18–26.