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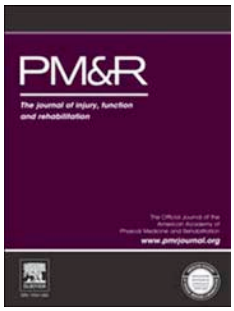

Autologous platelet-rich plasma versus dextrose prolotherapy for the treatment of chronic recalcitrant plantar fasciitis

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Title:

Autologous platelet-rich plasma *versus* dextrose prolotherapy for the treatment of chronic recalcitrant plantar fasciitis

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Autologous platelet-rich plasma *versus* dextrose prolotherapy for the treatment of chronic recalcitrant plantar fasciitis

ABTRACT

Objective: To determine the efficacy of autologous platelet-rich plasma (PRP) compared with dextrose prolotherapy (DP) in patients with chronic recalcitrant plantar fasciitis (PF)

Design: A single-blinded, randomized, controlled study

Setting: Department of Physical Medicine and Rehabilitation of University Hospital

Participants: Twenty-one patients with a clinical diagnosis of chronic PF confirmed by diagnostic ultrasound (plantar fascia thickness > 4 mm) were randomly assigned to the PRP group (n=10) or the DP group (n=11).

Interventions: Each patient received two injections into the plantar fascia through a peppering technique under ultrasound guidance at an interval of 2 weeks either with 2 ml of autologous PRP or 2 ml of 15% dextrose/lidocaine solution.

Main Outcome Measurements: The outcome measures included the pain, disability, and activity limitation subscales, measured by means of the Foot Functional Index (FFI). The data were collected before the first injection, at 2 weeks (before the second injection), and at the 2- and 6-month follow-ups.

Results: All patients completed the follow-up, with the exception of one patient in the PRP group. The mean FFI total and subcategory score improvements were larger in the PRP group compared with the DP group (improvement with PRP *vs*. DP – total: 30.4% *vs*. 15.1%, pain: 29.7% *vs*. 17.1%, disability: 26.6% *vs*. 14.5%, activity limitation: 28.0% *vs*. 12.4%). However, no statistically

significant difference was noted at all follow-up intervals. In the pain and disability subcategories, both groups showed significant improvements at the last re-evaluation interval. The PRP group also showed significant improvements in the disability and activity limitation subscales at the second re-evaluation interval.

Conclusions: Each treatment seems effective for chronic recalcitrant PF, expanding the treatment options for patients in whom conservative care failed. Additionally, PRP treatment may lead to a better initial improvement in function compared with DP treatment.

Key words: Platelet-rich plasma; dextrose prolotherapy; plantar fasciitis; Foot Functional Index

INTRODUCTION

Plantar fasciitis (PF) is the most common cause of heel pain〔1〕. The diagnosis is usually clinical and rarely needs to be investigated further〔2〕. Ultrasonography can be used to confirm recalcitrant PF or to exclude other pathology based on findings of proximal plantar fascia thickness greater than 4 mm and areas of hypoechogenicity〔3〕. Numerous treatments, including rest, weight loss, deep massage, stretching techniques, and heel cups usually start as patient-directed therapies and advance to nonsteroidal anti-inflammatory drugs, physical therapy, iontophoresis, night splint, and custom full-length arch supports as physician-prescribed therapies based on the response of symptoms over weeks **to** months〔1,3,4〕. These treatments are effective for ~90% of cases within this timeframe; therefore, some authors have suggested that PF represents a self-limiting condition without explicit proof of a treatment benefit over a wait-and-see approach〔2-

5〕. However, approximately 10% of patients remain recalcitrant to conservative therapies, necessitating further aggressive procedures such as injection therapy, extracorporeal shock wave therapy, and in some cases surgical release of the plantar fascia〔2,3,6〕. The efficacies of these treatments have been evaluated in systematic reviews, but the evidence for their effectiveness is limited**〔7-9〕**.

PF results from a degenerative process in the plantar fascia at its calcaneal attachment〔2〕. In fact, the pathology of chronic cases is characterized by an angiofibroblastic hyperblastic tissue that spreads throughout the surrounding tissue, creating a self-perpetuating cycle of degeneration〔10〕. Corticosteroid injections are a commonly used invasive procedure for the treatment of PF. However, the effect seems to be limited and short-lived, and further the use of corticosteroids is not a pathology-based therapy and has associated with the risks of fat pad atrophy and rupture of plantar fascia〔2-4〕.

Prolotherapy with dextrose (DP) has been reported to decrease pain and improve function in a variety of tendinopathies〔11,12〕. A potential biological effect of prolotherapy is supported by several clinical and animal studies, although the historical hypothesis that prolotherapy causes an inflammatory response leading to reduced tendon and ligament laxity has not been confirmed 〔5,13-17〕. Hyperosmolar dextrose has been shown to increase platelet-derived growth factor expression and up-regulate multiple mitogenic factors that may act as signaling mechanisms in

tendon repair〔18-20〕. Autologous platelet-rich plasma (PRP) injection is a relatively new modality. It aims to augment the natural healing process of tendon repair and regeneration by delivering high concentrations of growth factors directly to a lesion〔21〕. When platelets become activated, growth factors are released and initiate the natural healing process〔1,22,23〕.

With the encouraging biological basis and theory of DP and PRP injection for chronic PF, a few studies have suggested the beneficial effects of these therapies on the outcome of PF 〔5,6〕. However, currently, the applicable data are insufficient to support their routine clinical use. Furthermore, no trial has directly compared the efficacy of these two techniques in chronic recalcitrant PF. Therefore, the first aim of this study was to investigate the effectiveness of DP and PRP injection for treatment of chronic recalcitrant PF, and the second was to compare the efficacies of the two therapies.

METHODS

Patients and study design

The present study was designed as a single-blinded, randomized, controlled trial in patients with PF. Patients with a clinical diagnosis of chronic recalcitrant PF who were referred to the Department of Physical Medicine and Rehabilitation in the University General Hospital by general practitioners or orthopedic surgeons working in the same hospital were recruited. All patients included in the trial had to have had unilateral foot symptoms for a minimum of 6 months and had previously failed

therapy using conservative measures such as nonsteroidal anti-inflammatory drugs, stretching and physical therapy, night splint, arch supports, corticosteroid injections, and extracorporeal shock wave therapy. To confirm the diagnosis, the thickness of the proximal plantar fascia was measured by ultrasound at the inferior calcaneal border, and patients with a plantar fascia thickness ≥ 4 mm were included. Patients were excluded from the study if they received local steroid injections within 6 months or nonsteroidal anti-inflammatory drugs within 1 week prior to randomization. They were also excluded if they had cardiovascular, renal, or hepatic disease, diabetes, anemia, vascular insufficiency, peripheral neuropathy, active bilateral PF, or previous surgery for PF.

Randomization was performed after patients were deemed eligible and had provided informed consent. Patients with an odd sequence number were randomly allocated to the dextrose prolotherapy group; the following patient was automatically placed in the autologous PRP group. This study was approved by the committee for ethics in research at our institute, and was conducted in accordance with the World Medical Association Declaration of Helsinki.

Treatment procedures

Twenty milliliters of whole blood were collected from the antecubital fossa into a 25-mL syringe that contained 2 mL of anticoagulant (Huons ACD-soln®; sodium citrate 22 mg, citric acid 7.3 mg, glucose monohydrate 24.5 mg). The blood was then prepared according to the instructions of the Huons HC-1000 System® (Huons Co. Ltd., Sungnam, South Korea). This device is a centrifuge with disposable hourglass-shaped cylinders for the blood, within which approximately 0.05 mL of platelet concentrate is obtained from each patient. Autologous platelet concentrate contains concentrated white blood cells and platelets (buffy coat) after centrifugation at $3200 \times g$ for 3 min in

the neck of the cylinder. The buffy coat was extracted from the cylinder, and then 2 mL of supernatant plasma (platelet-poor plasma) was added, resulting in the final preparation for PRP injection. No activating agent was used. To estimate the concentration of the PRP extraction, blood samples of 10 healthy volunteers (normal blood test parameters) were examined. The resulting platelet concentration was found raised to be $(1{,}303 \pm 111.9) \times 10^3/\mu L$ (~7.6-fold platelet concentration compared to baseline whole blood).

The solution used for DP was a combination of 1.5 mL of 20% dextrose and 0.5 mL of 0.5% lidocaine, resulting in a 15% dextrose solution, within a 2.5-mL syringe. As part of the single-blind study, blood was also collected from the patients in the DP group. All preparation procedures were performed in the clinic without the patient present, by the same investigator (Kim E, MD, PhD; a physiatrist with 18 years' experience and more than 10,000 ultrasound-guided injections performed). The syringes for both DP and PRP were masked with opaque tape to ensure the patient was blinded throughout the trial.

The plantar fascia was examined on a treatment table using a 3-12 MHz real-time linear-array transducer (HD11XE, Philips Medical System, Bothell, WA). The injection procedure was performed under aseptic conditions using a 22-G needle. Abnormal hypoechoic areas in the thickened proximal plantar fascia were targeted under the longitudinal plane of ultrasound guidance, and the needle was inserted through the medial heel along the long-axis view (in-plane technique) toward the target area. Then, ~2 mL of PRP or dextrose solution was injected using a peppering technique, which involved a single skin portal followed by five penetrations of the fascia.

Immediately after injection, the patient was kept in the sitting position without moving the foot for

30 min. Patients were sent home with instructions to limit the use of their feet (allowing only indoor activities of daily living) for approximately 72 h and to use acetaminophen for pain. The use of nonsteroidal anti-inflammatory drugs and any type of foot orthoses was not allowed. Patients were also instructed to refrain from any heavy loading activity during the week following the procedure. Both groups of patients had a second course of injections at 2 weeks. At 4 weeks (2 weeks after the second injection), patients were allowed to proceed with activities of daily living or normal sports activities, as tolerated.

Outcome measures

Treatment evaluation was performed using the Foot Function Index (FFI), which was developed to measure the impact of foot pathology on function〔24〕. It consists of 23 self-reported items divided into three subcategories; pain, disability, and activity limitation. The patient scored each question on a scale from 0 (no pain or difficulty) to 10 (worst pain or so difficult it requires help). The pain subcategory consists of nine items and measures foot pain in different situations. The disability subcategory consists of nine items and measures difficulty performing various functional activities because of foot problems, such as difficulty walking four blocks. The activity limitation subcategory consists of five items and measures limitations in activities, such as using assistive devices outdoors because of foot problems. The FFI has been shown to have a high degree of internal consistency (Cronbach's alphas of 0.96–0.73) and test-retest reliability (intraclass correlation coefficients of 0.87–0.69), suggesting strong correlations between FFI total and sub-scale scores and clinical measures of foot pathology〔24〕. The FFI was administered prior to the first injections, at 2 weeks (before the second injections), at 10 weeks (2 months after the second

injections), and at 28 weeks (6 months after the second injections). All adverse events were recorded during follow-up.

Statistical analysis

All statistical analyses were performed using the SPSS software (ver. 14.0, SPSS Inc., Chicago, IL). Because of the small sample size, non-parametric tests were used to evaluate changes in the FFI total and sub-scale scores. The Mann-Whitney test was used to examine the effects of treatments between groups. The Wilcoxon signed-ranks test was used to evaluate changes in scores within groups. A value of $p<0.05$ was considered to indicate statistical significance. All data are expressed as means ± standard deviation.

RESULTS

Twenty-one consecutive patients with PF fulfilled the inclusion criteria and were enrolled in the trial. Eleven patients were randomly assigned to the DP group and 10 to the PRP group. Age, gender, height, weight, duration of symptoms, and occupation did not differ substantially between the two groups. Results of the randomization and the characteristics of patients are presented in Table 1. All patients completed the follow-up, with the exception of one patient in the PRP group who was lost to follow-up after the first injection, resulting in nine patients in the PRP group. Most patients in both groups reported local pain or discomfort that started on the day of injection and subsided gradually. With the exception of the above, no other complications of either injection therapy were reported in the patient groups.

An improvement in the mean FFI total scores from 132.5 ± 31.1 at baseline to 123.7 ± 47.4 (3.8% improvement) at 10 weeks and to 97.7 ± 52.5 (15.1% improvement) at 28 weeks follow-up was obtained in the DP group. The mean FFI total scores decreased from 151.5 ± 37.9 at baseline to 123.8 ± 45.4 (12.1% improvement) at 10 weeks and to 81.6 ± 55.3 (30.4% improvement) at 28 weeks in the PRP group (Figure 1). Regarding relative improvements in the scores, the PRP group showed better outcomes compared with the DP group at all re-evaluation intervals. However, there were no significant differences between groups at all follow-up intervals. Significant improvement was observed at the last re-evaluation interval in the DP group and at all intervals in the PRP group.

The mean pain subscale scores were 56.5 ± 14.0 at baseline, 52.5 ± 18.0 (4.5% improvement) at 10 weeks, and 41.1 ± 21.4 (17.1% improvement) at 28 weeks for the DP group and 60.4 ± 14.7 at baseline, 51.9 ± 17.6 (9.4% improvement) at 10 weeks, and 33.7 ± 23.4 (29.7% improvement) at 28 weeks for the PRP group. (Figure 2) The DP group showed improvement in mean disability subscale scores, from 53.4 ± 15.7 at baseline to 50.9 ± 22.4 (2.7% improvement) at 10 weeks and to 40.3 ± 21.8 (14.5% improvement) at 28 weeks in comparison to the PRP group, in which scores decreased from 55.8 ± 19.5 at baseline to 49.2 ± 19.4 (7.3% improvement) at 10 weeks and 31.9 ± 22.4 (26.6% improvement) at 28 weeks (Figure 3). The mean activity limitation subscale scores were 22.6 ± 9.8 at baseline, 20.4 ± 10.4 (4.4% improvement) at 10 weeks, and 16.4 ± 12.9 (12.4% improvement) at 28 weeks for the DP group and 31.3 ± 10.2 at baseline, 22.7 ± 11.2 (17.2% improvement) at 10 weeks, and 17.3 ± 11.6 (28.0% improvement) at 28 weeks for the PRP group (Figure 4). No significant differences in the FFI subcategory scores were noted between groups at all follow-up intervals. Both groups showed significant improvements in the pain and disability subscales at the last re-evaluation interval. The PRP group also showed significant improvement in the disability and activity limitation subscales at the second re-evaluation interval.

DICUSSION

The results of this study appeared to show the beneficial effects of both DP and PRP injection therapies in patients with chronic recalcitrant PF, with improvements in both pain and function. Compared to DP, PRP injection resulted in better outcomes in FFI total scores from baseline during the re-evaluation intervals. In terms of functional subcategories, improvement in the disability and activity limitation subscales was also evident at the earlier re-evaluation interval (after the second injection therapy) in the PRP group. The relative improvement in the pain subcategory was greater in the PRP group than in the DP group, although no significant difference was noted between the groups. A significant reduction in pain was found at the last re-evaluation interval (between 10 and 28 weeks) in both groups and, therefore, both treatments appeared to reduce pain in a few months after the injections. The effects of both treatments lasted throughout the follow-up period of this trial.

Regarding the initial 2 weeks between repeat injections as a treatment period, we considered the rest period (after the second injections at 2 weeks) to be an evaluation period during which the effects of both therapies would be exerted. Therefore, we set the re-evaluation times at 10 weeks (2 months after treatment) and 28 weeks (6 months after treatment). The improvements in the mean FFI total scores were 2.7% during the treatment period and 9.4% during the 2 months after treatment, resulting in 12.1% improvement at 10 weeks in the PRP group. The improvements in the mean FFI total scores were 4.1% and -0.3%, respectively, a 3.8% improvement, in the DP group. Disability and activity limitation scores showed significant decreases **within the 2 months** after treatment in the PRP group. On the other hand, the DP group did not demonstrate significant improvements in

any of the subcategory scores during this time. Moreover, the mean disability score increased (-2.6%) during this period in the DP group. In this trial, therefore, PRP treatment seemed to be effective for functional improvement in the short term, compared with DP. One possible explanation for this early effect could be that platelets improve the early neotendon properties so that the cells can perceive and respond to mechanical loading at an early time point〔25〕. Additionally, previous clinical studies of lateral epicondylosis have reported significant functional improvement after PRP treatment at 4–8 weeks, which is in agreement with our results〔22,23,26,27〕.

PF causes pain and tenderness under the heel and is a common condition that can lead to significant disability〔4〕. While acute cases of PF are characterized by the classical sign of inflammation, inflammation is not the underlying tissue disruption in more chronic PF cases〔1〕. In fact, the underlying pathology in PF is a degenerative tissue condition that occurs near the site of origin of the plantar fascia at the medial tuberosity of the calcaneus〔28〕. Numerous treatments have been used to manage PF, which indicates the lack of a curative therapy. When previous conservative treatments result in an unsatisfactory outcome, the patient is often interested in treatment options other than surgery. One treatment widely used in clinical practice is local corticosteroid injection, which is effective only in the short term and to only a limited degree〔1-4〕. It is also associated with a high frequency of recurrence, and direct pain relief after injection results in a tendency to overuse the affected foot〔4,29〕.

Prolotherapy involves injection of a small volume of proliferant at multiple sites around a ligament or tendon insertion〔5〕. Although several agents have been used, hyperosmolar dextrose is the most popular〔13〕. The proliferative response to dextrose is speculated to be a result of the higher osmolarity of the injected solution relative to the interstitial tissue. Evidence suggests stimulation of release of transforming growth factor β-1, platelet-derived growth factor, connective tissue growth factor, epithelial growth factor, and basic fibroblastic growth factor from mesangial cells, smooth muscle cells, and gingival fibroblasts upon exposure to various glucose concentrations 〔19,20,30,31〕.

Recently, the prevalence of the use of autologous blood products has been increasing; these might provide cellular and humoral mediators that enhance tissue healing in a variety of applications 〔32〕. PRP is promoted as an ideal autologous biological blood-derived product that can be applied exogenously to various tissues, where it releases high concentrations of platelet-derived growth factors〔1〕. Much laboratory evidence suggests that PRP can stimulate processes associated with tendon healing〔33〕. Indeed, in the past few years, clinical studies of PRP for the treatment of some tendinopathies have reported promising results〔22,23,26,27〕. Therefore, the injection of PRP into the plantar fascia could enable the healing necessary to reverse the degenerative process, as the pathologic nature of chronic recalcitrant PF is angiofibroblastic hyperplasia with degeneration at the origin of the proximal plantar fascia〔10〕.

Both therapies are being used increasingly commonly for various tendinopathies〔5,14,22,23,26〕. They may interrupt the degenerative cycle associated with tendinopathy and enable the native healing process, ultimately leading to improved clinical outcomes. In particular, the use of PRP is being studied intensely, and reports suggest that its clinical use for tendinopathies is increasing gradually〔13,21〕. However, each has been little assessed with regard to chronic PF〔5,6〕. Moreover, no trial has directly compared the effectiveness of the two treatments in tendinopathy, including chronic PF. In this trial, therefore, we compared the clinical outcomes of each technique for the treatment of recalcitrant PF. We focused on the potential benefits of PRP treatment on chronic PF in comparison with hyperosmolar dextrose; PRP treatment resulted in earlier functional improvement than DP treatment.

The natural history of non-chronic PF is benign, and symptoms usually improve within one year regardless of treatment although the time taken for the symptoms to resolve is highly variable 〔2,3〕. All patients enrolled in this trial had symptoms for at least 1 year (mean symptom durations in DP and PRP groups were 2.9 years and 2.8 years, respectively). Therefore, we believe that conservative therapies resulted in no improvement in these patients and that spontaneous resolution did not occur during the evaluation period.

DP treatment generally includes two to five injection sessions at 2- to 6-week intervals 〔5,14,17,34〕. PRP therapy protocols involving one, two, or more injections have been reported 〔26,35,36〕. Although DP requires a greater number of injections than PRP, which generally

requires a single injection〔21〕, we used a two-injection protocol for both treatments to make the conditions identical and maintain patient blinding. Additionally, repeated PRP injections may be beneficial in patients with suboptimal results after the initial injection〔22〕.

The use of ultrasound in injection therapies in clinical practice has become increasingly popular, due especially to performance of invasive procedures with better targeting of anatomical structures. In this trial, we administered intrafascial injections of both DP and PRP under ultrasound guidance to perform accurate injections without technical errors, and therefore, to ensure that the peppering technique used in both injection procedures was identical.

No activation was used during the procedure, as activation of platelets takes place *in vivo* after contact with thrombin, which is released from tissue collagen during the peppering technique 〔22,37〕. However, the dry needling used as part of the peppering technique itself has therapeutic effects that may have confounded our results〔21,26〕. Thus, we cannot conclude that the beneficial effects resulted solely from the hyperosmolar dextrose or PRP injection. Nonetheless, because the peppering technique, which was performed identically in both groups, is a fundamental component of both treatments, the beneficial outcomes are attributable to the effects of the treatments.

As a technique that places injectant on a degenerative area of the plantar fascia or bony attachment, each technique and injectant appeared safe. To date, no study of these therapies for musculoskeletal conditions has reported serious adverse events〔5,6,22,23,26,27〕. Some believe that growth

factors act in a dose-dependent manner, although no data indicating the quantity of growth factors necessary to stimulate healing are to our knowledge extant. Studies have shown that clinical efficacy can be expected with a minimum increase in platelet concentration of 4- to 6-fold from the whole blood baseline〔38,39〕. In this trial, we achieved an average increase in platelet concentration 7.6-fold that of the baseline.

Alternatively, the beneficial effects of a blood-derived preparation may be affected by plasma-derived biologically active substances and/or other blood cells, such as white blood cells, present in whole blood; this issue has received little attention〔40〕. We used a high-yield PRP preparation containing concentrated white blood cells (buffy coat). The presence of an elevated concentration of leukocytes in the PRP is a current topic of interest. Leukocytes are thought to generate an antibacterial response and can debride dead tendon tissue and jump-start healing because they also produce growth factors〔23〕. However, whether the increased number of leukocytes in the PRP has a positive effect on PF is not known because no comparative data have been published to date.

One of the limitations of this study is the relatively small number of cases included. Thus, the small population size of this trial prevents a consensus recommendation on the use of either of the treatments at this time. This trial was not placebo-controlled, as it was not considered ethical to include a sham placebo control group, i.e., dry-needling group; thus the placebo effect cannot be ruled out. Additionally, this was a single-blinded study; hence, the introduction of bias at the treatment stage also cannot be ruled out. However, patients were blinded to treatment throughout the study, and separate investigators evaluated the outcome measures, in an attempt to minimize

bias. The 6-month follow-up may be considered short, but we believe that our data indicated an enduring benefit of both treatments at the re-evaluation time points used. Despite the limitations, we demonstrated that DP and PRP are safe, relatively simple, and potentially effective methods of improving the outcomes of chronic, recalcitrant PF.

CONCLUSIONS

To our knowledge, this is the first report to compare PRP injection with DP as a treatment for chronic recalcitrant PF. Our data demonstrate that injection of DP and PRP improved pain and function mainly after two months of both treatments, and the improvements were sustained over time with no reported complications. Therefore, both therapies appeared effective for recalcitrant PF, thus expanding treatment options for patients in whom conservative care has failed. Additionally, in this trial, PRP treatment resulted in a better initial improvement in function compared with DP treatment. However, our results raise the question whether a higher concentration of growth factors should be administered directly to a degenerative lesion site to stimulate healing, because hyperosmolar dextrose appeared eventually to be as efficacious as a high concentration of platelets. Accordingly, further studies using validated clinical measures with a large population, and radiological and biological findings as secondary outcome measures, are needed. These should also elucidate more specific indications for PRP treatment, including the optimum PRP concentration and the presence or absence of white blood cells, and the number and frequency of injections needed for chronic recalcitrant PF and other tendinopathies.

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448 **Figure Legends**

449

450 **Figure 1.** Improvement in Foot Functional Index (FFI) total scores across assessment points (values
451 are means ± standard deviation in parentheses). [a] indicates the *p*-value from the Wilcoxon signed-
452 ranks test used to evaluate changes in FFI total scores between assessment points within groups; [b]
453 indicates the *p*-value from the Mann-Whitney test used to examine the effects of treatment on total
454 scores between groups at each assessment point.
455 DP, dextrose prolotherapy; PRP, platelet-rich plasma.
456

457 **Figure 2.** Improvement in Foot Functional Index (FFI) pain subscale scores across assessment
458 points (values are means ± standard deviation in parentheses). [a] indicates the *p*-value from the
459 Wilcoxon signed-ranks test used to evaluate changes in pain scores between assessment points
460 within groups; [b] indicates the *p*-value from the Mann-Whitney test used to examine the effects of
461 treatment on pain scores between groups at each assessment point.
462 DP, dextrose prolotherapy; PRP, platelet-rich plasma.
463

464 **Figure 3.** Improvement in Foot Functional Index (FFI) disability subscale scores across assessment
465 points (values are means ± standard deviation in parenthesis). [a] indicates the *p*-value from the
466 Wilcoxon signed-ranks test used to evaluate changes in disability scores between assessment points
467 within groups; [b] indicates the *p*-value from the Mann-Whitney test used to examine the effects of
468 treatment on disability scores between groups at each assessment point.
469 DP, dextrose prolotherapy; PRP, platelet-rich plasma.

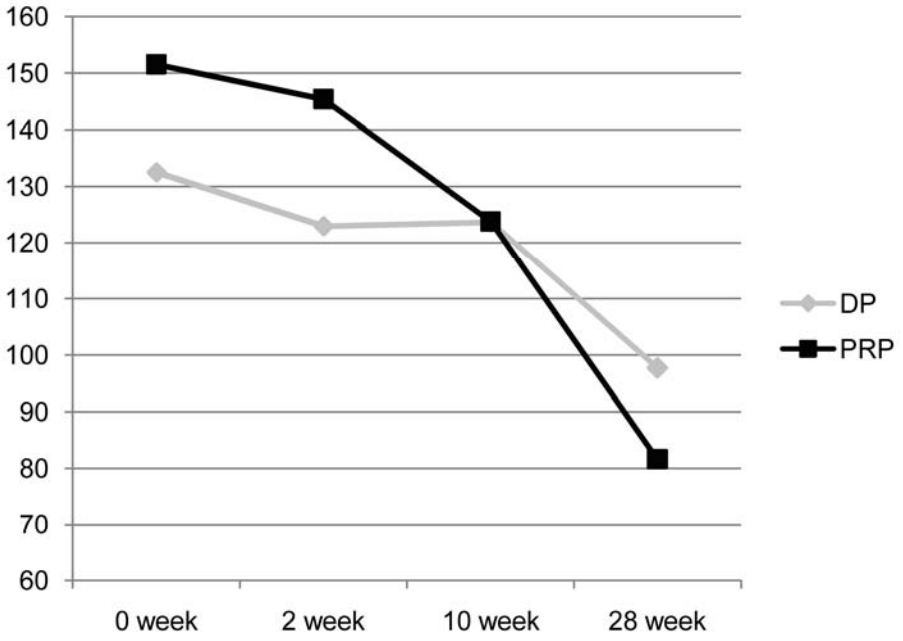
Figure 4. Improvement in Foot Functional Index (FFI) activity limitation subscale scores across assessment points (values are means ± standard deviation in parentheses). [a] indicates the *p*-value from the Wilcoxon signed ranks test used to evaluate changes in activity limitation scores between assessment points within groups; [b] indicates the *p*-value from the Mann-Whitney test used to examine the effects of treatment on activity limitation scores between groups at each assessment point.

DP, dextrose prolotherapy; PRP, platelet-rich plasma.

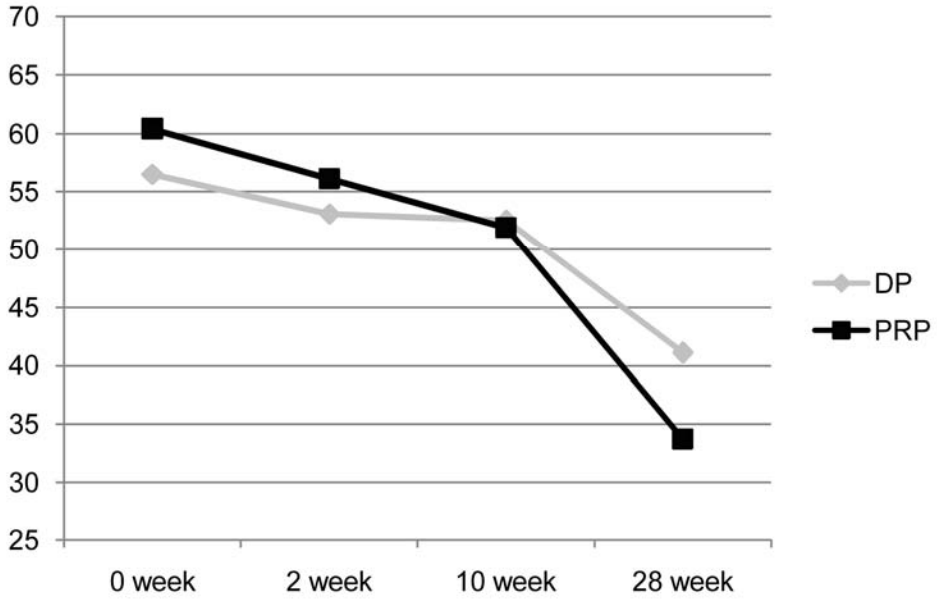
Table 1. Characteristics of Patients

Group	Number	Age (range), year	Gender, Female/Male	Height (SD), cm	Weight (SD), kg	Lesion, Left/Right	Duration (range), year	Occupation: office/ labor/housekeeping
DP	11	37.8 (19-51)	4/7	169.5 (7.6)	64.7 (12.2)	5/6	2.9 (1-6)	8/1/2
PRP	10	36.2 (20-57)	6/4	167.2 (7.9)	60.0 (10.1)	5/5	2.8 (1-6)	6/1/3

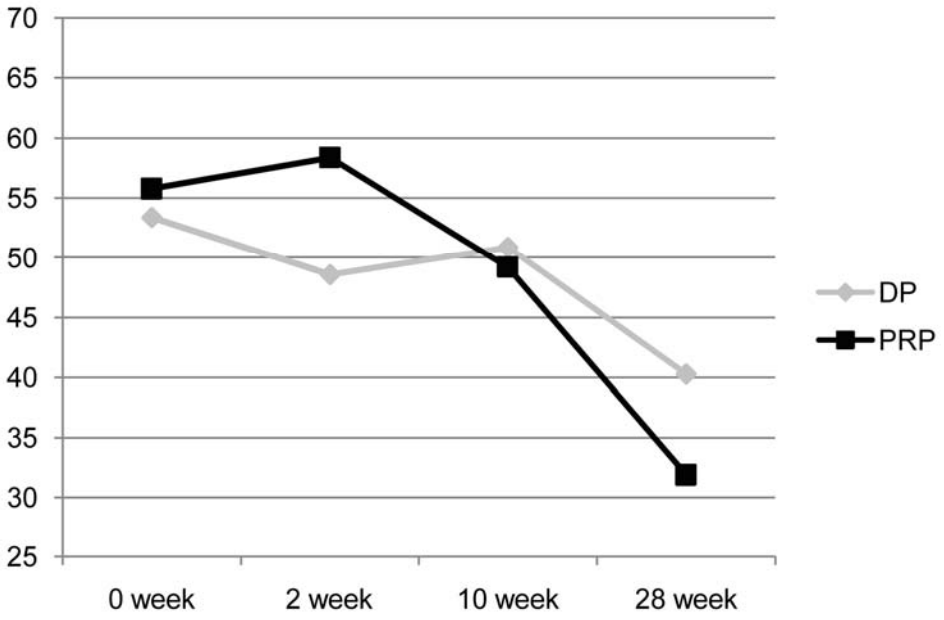
DP, dextrose prolotherapy; PRP, platelet-rich plasma; SD, standard deviation



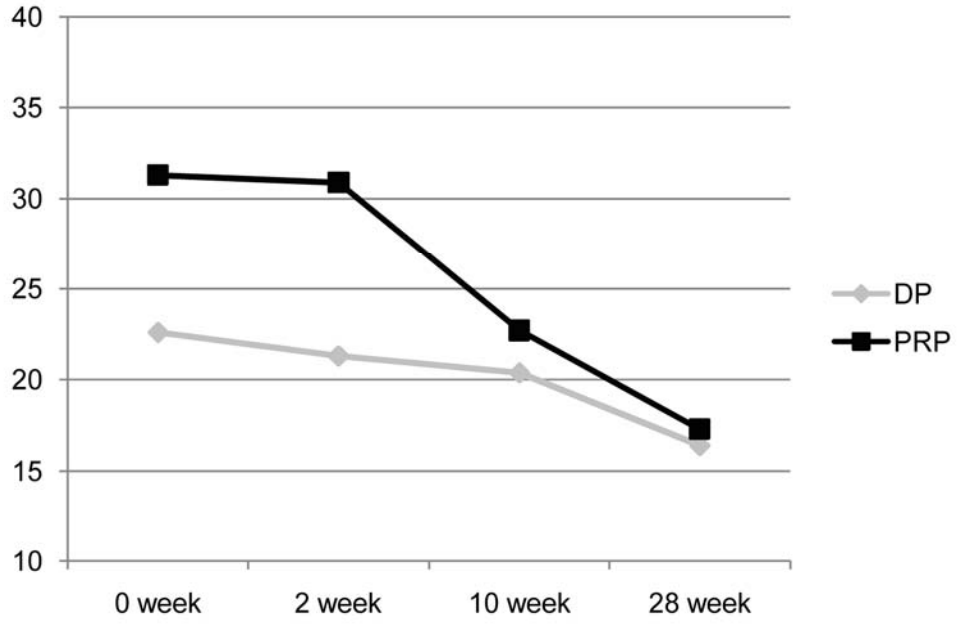
Group	0 week	p^a	2 week	p^a	10 week	p^a	28 week
DP (n=11)	132.5 (31.1)	0.182	123.0 (42.8)	0.646	123.7 (47.4)	0.011	97.7 (52.5)
PRP (n=9)	151.5 (37.9)	0.024	145.4 (43.4)	0.036	123.8 (45.4)	0.038	81.6 (55.3)
p^b	0.251		0.295		0.882		0.603



Group	0 week	p^a	2 week	p^a	10 week	p^a	28 week
DP (n=11)	56.5 (14.0)	0.247	53.1 (16.6)	0.824	52.5 (18.0)	0.008	41.1 (21.4)
PRP (n=9)	60.4 (14.7)	0.075	56.1 (19.6)	0.476	51.9 (17.6)	0.038	33.7 (23.4)
p^b	0.605		0.766		0.941		0.412



Group	0 week	p^a	2 week	p^a	10 week	p^a	28 week
DP (n=11)	53.4 (15.7)	0.422	48.6 (19.6)	0.541	50.9 (22.4)	0.010	40.3 (21.8)
PRP (n=9)	55.8 (19.5)	0.374	58.4 (19.9)	0.042	49.2 (19.4)	0.028	31.9 (22.4)
p^b	0.863		0.261		0.882		0.552



Group	0 week	p^a	2 week	p^a	10 week	p^a	28 week
DP (n=11)	22.6 (9.8)	0.283	21.3 (10.7)	0.682	20.4 (10.4)	0.173	16.4 (12.9)
PRP (n=9)	31.3 (10.2)	0.313	30.9 (9.7)	0.013	22.7 (11.2)	0.116	17.3 (11.6)
p^b	0.061		0.080		0.766		0.941