Original Research Article

Comparison of the effectiveness of platelet rich plasma and ozone therapy in plantar fasciitis treatment

Umit Yalcin*

Department of Physical Medicine and Rehabilitation, Medicana International Istanbul Hospital, Beylikduzu, Istanbul, Turkey

Received: 06 April 2020
Accepted: 29 April 2020

*Correspondence:
Dr. Umit Yalcin,
E-mail: drumiftr07@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Plantar fasciitis (PF) is one of the most common foot problems in adults. Conservative treatments are proportionally 90-95% successful. In this study, author aimed to compare the effectiveness of ozone therapy (OT) treatment of platelet rich plasma (PRP) injections in PF patients.

Methods: In the study, which was made prospectively, patients were randomly divided into two groups. In the first group (n=20), patients were injected with PRP in 3 sessions at a one week intervals, and in the second group (n=22) OT was injected in the same way. Each patient was evaluated with visual pain score before as well as 1 month after treatment in terms of pain, whereas the foot function index (FFI) was evaluated with the score in terms of functionality.

Results: In both groups, the 1st month VAS score and FFI score showed significant decrease (p<0.05) after treatment compared to before treatment. The decrease in VAS score and FFI score after treatment in the PRP group was significantly higher than the OT group (p<0.05).

Conclusions: As a result of this study, authors found that both PRP and OT were beneficial in terms of pain and functional level in the treatment of PF, but in patients who underwent PRP, authors found that there was more statistical improvement in terms of both parameters than patients who received OT. In light of the absence of a previous publication comparing these two treatment options in PF treatment, this study contributes to the literature.

Keywords: Complementary medicine, Plantar fasciitis, Pain, Platelet rich plasma, Ozone therapy

INTRODUCTION

Heel pain is one of the most common foot problems in adults. It occurs in about 10% of the population, throughout life. It can be bilateral in approximately 20- to 30% of patients.1-2 Although the exact etiology is not clear, it is more common in obese people, those who remain standing for a long time and in runners. In addition, factors such as trauma, improper footwear, decreased ankle dorsiflexion, impaired biomechanical factors and flat foot soles are thought to play a role.2 PF is the most common cause of chronic pain on the lower half of the heel that occurs without a traumatic cause. The average PF rate of patients with heel pain is 53.2%. PF are the changes occurring in the plantar fascia as a result of chronic inflammation and tears.3,4 The plantar fascia is a multi-layered fibrous band located deep below the fat layer on the sole of the foot and extends from the medial plantar tubercle of the calcaneus to the base of the toes. It supports the medial longitudinal arch of the foot. Plantar fascia creates a static support for the longitudinal arc of the foot and although it is limited as a shock absorber with increasing load, it results in elongation.5-6 Repetitive microtraumas in the plantar fascia cause traction peristitis, micro rupture and degenerative changes. Pain associated with PF occurs gradually and most prominently when getting up in the morning, after getting out of bed or standing still for a long time. Pain is
often described in the proximal of the medial longitudinal arch of the heel, around the medial tubercle, in the adhesion of the plantar fascia.\textsuperscript{2,4} It becomes subtler after a few steps, but intensifies towards the end of the day, depending on loading and activity. The pain decreases with rest, but it resumes again in the first step after rest. Sometimes mild swelling and erythema can be seen. The duration of symptoms can vary from a few weeks to years.\textsuperscript{7}

Diagnosis of PF can be made with the patient’s history, physical findings, detection and intensification of pain by examination, if necessary, forefront, back and standing side radiographs of the heel, ultrasonography and magnetic resonance imaging.\textsuperscript{4,8} Treatment methods in PF are divided into two, namely surgical and conservative. Conservative treatment is 90-95% successful, therefore, the surgical method should be preferred firstly.\textsuperscript{9,10} Stretching exercises, splints, orthoses, nonsteroidal anti-inflammatory drugs, steroid injections and extracorporeal shock wave therapy (extracorporeal shockwave therapy, ESWT) are non-surgical treatment options.\textsuperscript{3} Since local steroid injections increase the risk of rupture in PF treatment, surgical methods are less preferred due to possible complications. Ideal non-surgical treatment in PF treatment should have as many effective and minimal complications as other treatment options. One of the treatment options is platelet-rich plasma injection (PRP). PRP is a form of treatment that stimulates natural healing steps through growth factors in platelets. Applied to the injury site accelerates the physiological healing process, it provides support for the binding of cells, reduces pain and, has an anti-inflammatory as well as an antibacterial effect.\textsuperscript{11} With the FDA approval in 2012, PRP has been widely started to use in problems involving many musculoskeletal systems and studies are included in the literature on the use of PRP in PF and chronic tendinopathy.\textsuperscript{12,14} The purpose of using PRP in this degenerative and chronic process is turning a chronic injury into a new acute injury by restarting the inflammatory process interrupted by unsuccessful conservative treatment.\textsuperscript{15} High growth factors within PRP increase the regeneration ability and the regeneration process of tissue.\textsuperscript{16} Apart from ready-made kits, PRP can also be obtained manually from peripheral blood.\textsuperscript{17,18} At the same time, many questions regarding the ideal volume, frequency of application, application period and platelet activation regarding PRP administration have not been answered yet.\textsuperscript{19} Medical ozone is also a long-term treatment used contemporarily, though the amount of literature on this issue is very limited. Although its mechanism is not well known, it is thought to reduce pain and inflammation by blocking Tumor necrosis factor-a (TNFa) and phosphodiesterase A2.\textsuperscript{20} It has been proven beneficial in knee osteoarthritis, myofascial pain syndrome and many other diseases.\textsuperscript{21,22} Author did not find a prospective study comparing the effectiveness of PRP and OT in the treatment of PF. In this study, author examined the effects of these two treatment methods, which have been used frequently in recent years, on pain and physical function in PF.

**METHODS**

Included in this study were 46 patients between the ages of 20 and 65 who were admitted to the physical medicine and rehabilitation clinic with foot pain between November 2019 and April 2020, and diagnosed with PF. The patients were informed about the study and, their written consents as well as the ethics committee’s approval of this study were obtained. Throughout the study, the individual rights of the patients were observed, adhering to the Helsinki Declaration principles. The diagnosis of PF was made by clinical examination. Direct radiographs of the patients were checked to differentiate other pathologies related to the heel region. In the prospective study, patients were randomly divided into two groups by sing the sealed envelope method. In the first group (n=20), a total of 3 sessions of PRP were injected at one week intervals, and in the second group (n=22) OT was injected. Three patients from the first group and one from the second group were excluded from the study because they did not come for follow up. Each patient was evaluated with the VAS score in terms of pain and with the FFI score in terms of function, prior to treatment and 1 month after treatment.

**Inclusion criteria**

- 20 to 65 years of age, presence of heel pain for at least 4 weeks, diagnosis of CS, absence of medical treatment, injection, physical or surgical treatment for the last 4 weeks, volunteering.

**Exclusion criteria**

- Hemoglobin (Hb) value <11g/dL, platelet count <150, 000/mm\textsuperscript{3}, with a history of systemic disease, pregnancy, active tumor or hematological malignant disease, infection, anticoagulant use up to five days prior, the use of nonsteroidal anti-inflammatory drugs (NSAIDs), patients who had a history of steroid injection in the heel region, had a calcaneus fracture or had a history of surgery from the heel region, were all excluded from the study.

**Procedures**

Preparation and application of PRP was performed in all patients under the same conditions. A total of 10 cc of peripheral blood taken from the antecubital region was taken into tubes containing 3.2% sodium citrate. Samples were centrifuged (Eppendorf centrifuge 5702, Hamburg Germany) for 10 minutes at 3200 rpm at room temperature. The 2 ml of PRP obtained was applied to the most sensitive point by palpation to the medial region of the foot under sterile conditions. Additional treatments, such as orthoses, were not given until the study was
completed. This treatment was applied for a total of 3 sessions with an interval of 1 week.

In the second group, the same procedure was followed: 3 ml 20µg/ml OT with a 22 G needle to the most sensitive point with palpation were applied in 3 sessions with a 1 week interval. All patients were given a four-week exercise program, which included stretching exercises with the gastrocnemius and soleus muscles for the plantar fascia. The exercises, defined by the same doctor, called for 15 reps, a 10 seconds duration twice a day. The VAS score in terms of pain and the FFI in terms of functional status were examined prior as well as 1 month after the treatment, of patients in both groups.

**Statistical analysis**

Mean, standard deviation, median, minimum, maximum value frequency and percentage were used for descriptive statistics. The distribution of variables was checked with kolmogorov-simirnov test. Independent Samples t test and mann-whitney U test were used for the comparison of quantitative data. Paired samples t test and wilcoxon test were used for the repeated measurement analysis. Chi-Square test was used for the comparison of the distribution of qualitative data. SPSS 26.0 was used for statistical analyses.23-25

**RESULTS**

Sociodemographic characteristics are summarized in Table 1 (mean age 48.0±10.0 years). Of the patients, 28 were female (66.7%) and 14 were male (33.3%). The mean VAS and total FFI scores before the treatment were 6.9±1.3 and 71.3±13.9 respectively. No significant difference was found between the groups in terms of demographic characteristics, VAS and FFI scores at the beginning (p>0.05) (Table 2).

| Table 1: Demographic characteristics of patients. |
|-----------------|-----------------|-----------------|-----------------|
| Age             | Male            | Female          | Gender          |
| Age             | Mean±sd/n-%     | Median          | Mean±sd/n-%     | Median          |
| Gender          | 26.0-67.0       | 48.5            | 28-66.7%        |
| Gender          | 14-33.3%        |                 |                 |
| VAS Score       | 4.0-9.0         | 7.0             | 6.9±1.3         |
| Foot Function Index | 39.8-92.7     | 72.9            | 71.3±13.9       |

Min-minimum; max-maximum; sd-standart deviation; VAS-visual analog scale; FFI-foot function index

| Table 2: Comparison of demographic characteristics, VAS pain and FFI scores before and after treatment between groups. |
|-----------------|-----------------|-----------------|-----------------|
| Age             | PRP             | Ozone therapy   | Pr              |
| Age             | Mean±sd/n-%     | Median          | Mean±sd/n-%     | Median          | P   |
| Age             | 46.7±11.5       | 48.0            | 49.1±8.5        | 49.0            | 0.438 |
| Gender          | Female          | 13-65.0%        | 15-68.2%        | 0.827 |
| Gender          | Male            | 7-35.0%         | 7-31.8%         |                 |
| VAS Score       | Before Treatment| 7.2±1.1         | 7.0             | 0.149 |
| VAS Score       | 1st Month       | 1.8±1.4         | 1.5             | 4.0             | 0.000 |
| VAS Score       | 1st Month Difference | 5.4±1.8      | 6.0             | 3.0             | 0.000 |
| VAS Score       | Intra Group Difference p | 0.0000    |                 |                 |
| VAS Score       | Before Treatment| 72.9±12.0       | 72.9            | 73.4             | 0.468 |
| VAS Score       | 1st Month       | 20.7±14.3       | 22.7            | 42.5             | 0.001 |
| VAS Score       | 1st Month Difference | 52.2±18.2   | 59.5            | 33.0             | 0.001 |
| VAS Score       | Intra Group Difference p | 0.0000    |                 |                 |
| VAS Score       | 1st Month       | 20.7±14.3       | 22.7            | 42.5             | 0.001 |
| VAS Score       | 1st Month Difference | 52.2±18.2   | 59.5            | 33.0             | 0.001 |
| VAS Score       | Intra Group Difference p | 0.0000    |                 |                 |

In both groups, the first month VAS scores after treatment decreased significantly (p<0.05) compared to the pretreatment. The VAS scores decrease after treatment in the PRP group was significantly higher (p<0.05) than in the OT group (Table 2).

In both groups, the first month FFI scores decreased significantly (p<0.05) after treatment compared to pretreatment. The FFI scores decrease after treatment in the PRP group was significantly higher (p<0.05) than the OT group (Table 2).

**DISCUSSION**

Heel pain is the most common complaint relating to the foot. Many local and systemic causes can cause under-
heel pain. Heel pain is a clinical condition that is encountered frequently in almost every period of life, however, not all problems have yet been overcome in its diagnosis and treatment. PF is the most common cause of heel pain.26 The etiology of PF is not fully known, though according to the common held opinions in the literature, micro-tears caused by mechanical loading initiate an inflammatory response. In contrast to this information, Lemont et al. did not detect any signs of histological inflammation in PF histological samples.27 Furthermore, it is stated that most patients with PF can recover within one year without any treatment and the rate of recovery can reach 90% with conservative treatment. The first option in treatment is conservative methods. There are many non-surgical treatment options that give different results in PF treatment yet there is still no consensus on what is the ideal treatment option for PF. In PF treatment, concomitant deformaties and systemic diseases, if any, should be controlled. NSAIDs, corticosteroid injections together with local anesthetics can be tried to relieve pain. The local injection is usually done to or around the PF’s area of origin. Attenuation of the patient is important in treatment.28 Stretching exercises to PF, gastrocnemius and gastrosoleus muscles, shoe modifications, orthotic devices (foot and/ or foot-ankle orthoses), physical therapy, ESWT consist additional treatment options. Surgery can be considered in patients who do not respond to conservative treatment for 6 to 12 months.29 In the literature, steroid injection has been reported to be useful in the short term in the treatment of PF, however cases of plantar fascia rupture, fat pad atrophy, abscess, and osteomyelitis associated with steroid injections have been reported.30 In recent years, there is an increasing use of PRP in foot and ankle pathologies. PRP include Platelet-derived insulin-like growth factor (IGF), fibroblast growth factor (FGF), platelet-derived growth factor (PRGF), epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF). These factors suppress inflammation and by stimulating the removal of necrotic cells, assist tissue reconstruction. Due to these properties, many different disciplines have reported very successful results with this agent which has found its use not only in orthopedic pathologies, but in many different areas. There is no consensus on how often growth factor doses or concentrations should be applied. Sánchez et al., in a study in which they compared PRGF and hyaluronic acid (HA) injections with 176 patients, applied 3 injections of a total of 8ml of plasma one week apart, the composition of which they obtained after the procedure to the patients. With PRGF they achieved more improvement in pain and function. 31 Gülser et al., in a study where they compared PRP and HA injections with 175 patients, the patients received a total of 2ml of plasma and buffy coat composition with 3 injections after the procedure one week apart and they reported that they achieved more significant improvements in PRP and knee society score (KSS) scores and VAS scores compared to patients who underwent HA.32 Cerza et al., in a study where they compared PRP and hyaluronic acid (HA) injections with 120 patients, applied a total of 5.5ml plasma and buffy coat composition obtained after the procedure 4 injections with one week apart, and reported that they achieved more improvement in pain and function with PRP.33 In this study, authors applied 3 sessions of PRP injection 2 ml once a week. Three different methods can be used to obtain PRP: with automatic machines and ready kits, double-spin rotation, single-spin rotation and manually.24 The prepared PRP is activated by adding bovine or human thrombin or calcium chloride. With the formation of platelet gel from activated PRP, growth factors and cytokines are released. Some authors use PRP without activating it.16 In this study PRP has been prepared with ready kit (PRP S and M, STR Bio Medical Technologies, Çorum, Turkey). In the analysis of the prepared PRP, it was determined that it was 3 times more concentrated than the number of platelets in the peripheral blood, and calcium chloride was not added to the prepared PRP for activation. There are many studies in the literature regarding the use of PRP in plantar fasciitis and chronic tendinopathy. Barrett and Errede performed PRP in nine patients with ultrasonography (USG) and measured the plantar fascia thickness with USG. The authors found that after treatment, the thickness of the plantar fascia decreased and the signal intensity changed in USG, and that after one year, 77.9% of the patients were complaint-free.13 Although Akşahin et al., determined that the functional and pain scores of 30 patients who received steroids and 30 patients who received PRP were similar in the third week and 6 months, they suggested the use of PRP when considering steroid complications.31 In the study of Martinelli et al., it was reported that pain scores decreased after 12 months of follow-up in 14 patients who underwent PRP.16 When the findings of this study were evaluated, it was found that functional scores increased in a statistically significant way, compared to baseline values in the first month controls after application in both groups, whereas pain scores decreased in statistically significant way compared to baseline values. When the groups were compared with each other, it was seen that the change in function and pain scores in the PRP group were significantly better than in the ozone group. There is no risk of immune reaction or disease transfer for PRP obtained from autologous blood. There is also no study in the literature indicating that PRP may stimulate hyperplasia, carcinogenesis or tumor growth.11 In this study, authors did not encounter any complications in patients undergoing PRP.

The first use of ozone in medicine was carried out by Fisch in 1932 and Payer examined the contribution of OT to surgical treatment in 1935. Today, OT can be used in different branches with different indications. Ozone has found a place in the treatment of osteoarthritis with the increase in oxygenation after neoangiogenesis, its anti-inflammatory properties and its analgesic effect with its stimulation of the antinociceptive system.32 It is stated that by stimulating synovial tissue, it increases lubrication and supports cartilage repair. It increases
microcirculation by reducing compression and stasis in intra-articular vascular structures, thereby providing oxygenation and reduces emerging pain associated with neuronal hypoxia. The anti-inflammatory activity of ozone in the joint occurs depending on suppression of pro-inflammatory prostaglandin synthesis, inhibiting the release of bradykinin and increasing the release of pro-inflammatory cytokine antagonists. Intraarticular applications can be most common preferred in the knee joint, buttock, shoulder, ankle and other peripheral joints. It can be used in inflammatory, degenerative diseases and after sports injuries. Although a complete consensus has not been achieved regarding ozone/ oxygen concentrations and doses, studies suggest a 10-20μg/mL concentration 5-20 mL in the knee and shoulder joint, in the smaller joints, trigger points in the soft tissue and intramuscular weekly injections at concentrations of 10-15μg/ mL 2-3mL have been recommended. Similarly, in this study, authors applied ozone at a dose of 3ml 15μg/ml. Since randomized controlled trial with medical ozone are few and far between, it is quite difficult to make general conclusions about treatment results yet and in PF, there are no studies comparing OT and PRP this study will be the first in terms of this feature. There are a limited number of studies on OT in PF. One of them, Bahrami MH et al, a randomized controlled double-blind study in which 44 patients diagnosed with PF were evaluated and 40mg of methylprednisolone was injected into a first group and 3 ml of 15μg/mL ozone was injected into a second group. There was no difference between the two groups in terms of pain and functional level. In another study, Babaei-Ghazali et al, 30 patients diagnosed with PF were divided into two groups, the first group being treated with a methylprednisolone injection and OT being applied to the second group, both then followed for three months. As a result, they found that both methods were effective in the treatment of PF that and there was no statistically significant difference between the two groups.

**CONCLUSION**

In conclusion to this study, author found that both PRP and OT were beneficial in terms of pain and functional level in the treatment of PF, however author found that there was more improvement in both parameters in patients with PRP compared to patients who received OT. This study confirms that PRP and OT, which have been used frequently in medicine in recent years, are beneficial in terms of pain and functional recovery in PF treatment; and it contributes to the literature in terms of the absence of a previous publication comparing these two treatment options in PF treatment. Limitations of this study were absence of a placebo control group, the fact that there are no radiological and biological results, the manner of the evaluation of patients with their pain and physical function scores, as well as the low number of patients and the relatively short follow-up period.

**Funding:** No funding sources

**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

**REFERENCES**


