

A randomized study comparing the effect of platelet-rich plasma and platelet-poor plasma for the treatment of plantar fasciitis

Estudo aleatório comparando o efeito do plasma rico e plasma pobre em plaquetas para o tratamento de fasciitis plantar

Ensayo aleatorizado que compara el efecto del plasma rico en plaquetas y el plasma pobre en plaquetas para el tratamiento de la fascitis plantar

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Elcio Valotto-Junior

ORCID: <https://orcid.org/0000-0002-1385-2224>
Universidade Estadual de Maringá, Brazil
E-mail: vallotojr@yahoo.com.br

Sandra Bin Silva

ORCID: <https://orcid.org/0000-0002-2018-8341>
Universidade Estadual de Maringá, Brazil
E-mail: sandrabin@gmail.com

Luis Henrique Garcia Muniz

ORCID: <https://orcid.org/0000-0001-8683-496X>
Universidade Estadual de Maringá, Brazil
E-mail: lhgmuniz@uem.br

Fernanda Ferreira Evangelista

ORCID: <https://orcid.org/0000-0001-9576-3075>
Universidade Estadual de Maringá, Brazil
E-mail: fer.evangelista@hotmail.com

Luciano Henrique Gazoni Scremin

ORCID: <https://orcid.org/0000-0001-6387-0829>
Universidade Estadual de Maringá, Brazil
E-mail: screminmsk@gmail.com

Elisabete Mitiko Kobayashi

ORCID: <https://orcid.org/0000-0003-3770-4223>
Universidade Estadual de Maringá, Brazil
E-mail: emkwilson@uem.br

Elza Kimura

ORCID: <https://orcid.org/0000-0002-6466-5074>
Universidade Estadual de Maringá, Brazil
E-mail: ekimura@uem.br

Abstract

Objective: To verify the effectiveness of therapy with platelet-rich plasma (PRP) in patients with plantar fasciitis, this prospective, longitudinal, double-blind study was carried out. *Methodology:* Twenty-three participants with chronic plantar fasciitis aged > 20 years, already treated with conventional methods were included. Participants were randomly divided into platelet-poor plasma (PPP) and platelet-rich plasma (PRP) groups. Double centrifugation was carried out to prepare the platelets samples and two millilitres of PPP (supernatant fraction) or PRP (sediment fraction) were mixed with 1mL of 2% calcium gluconate solution and injected in the plantar fascia, as a single dose. A follow-up at 15 days and then every 60 days up to 180 days of application was carried out and a visual analogue scale (VAS) for pain assessment and the quality-of-life scale validated by the American Orthopedic Foot and Ankle Society (AOFAS) were used to measure the outcomes. *Results:* A reduction in pain (VAS 8 to 4), in both groups, was seen in the first 15 days and remained up to the 6th month after the application of plasmas, however, no difference was observed between the groups. No significant improvement was observed in the quality of life of the patients. *Conclusion:* PPP or PRP were able to reduce the VAS, but the presence of platelets did not have a role in the pain relief. Other factors in the plasma may play a role in reducing the pain caused by plantar fasciitis for a period of up to 180 days.

Keywords: Plantar Fasciitis; Pain; Platelet-rich plasma.

Resumo

Objetivo: para verificar a eficácia da terapia com plasma rico em plaquetas (PRP) em pacientes com fascite plantar, foi realizado este estudo prospectivo, longitudinal e duplo-cego. *Metodologia:* Foram incluídos 23 participantes com

fascite plantar crônica com idade > 20 anos, já tratados com métodos convencionais. Os participantes foram divididos, aleatoriamente, em grupos de plasma pobre em plaquetas (PPP) e plasma rico em plaquetas (PRP). Dupla centrifugação foi realizada para preparo das amostras de plaquetas e dois mililitros de PPP (fração sobrenadante) ou PRP (fração sedimentar) foram misturados a 1mL de solução de gluconato de cálcio 2% e injetados na fáscia plantar, em dose única. Foi realizado um acompanhamento aos 15 dias e depois a cada 60 dias até 180 dias de aplicação e foram aplicadas as escalas visuais analógicas (EVA) para avaliação da dor e a escala de qualidade de vida validada pela *American Orthopaedic Foot and Ankle Society* (AOFAS). usados para medir os resultados. *Resultados*: Houve redução da dor (EVA 8 para 4), em ambos os grupos, nos primeiros 15 dias e permaneceu até o 6º mês após a aplicação dos plasmas, porém não foi observada diferença entre os grupos. Não houve melhora significativa na qualidade de vida dos pacientes. *Conclusão*: PPP ou PRP foram capazes de reduzir a EVA, mas a presença de plaquetas não teve papel no alívio da dor. Outros fatores no plasma podem desempenhar um papel na redução da dor causada pela fascite plantar por um período de até 180 dias.

Palavras-chave: Fascite Plantar; Dor; Plasma rico em plaquetas

Resumen

Objetivo: para verificar la efectividad de la terapia con plasma rico en plaquetas (PRP) en pacientes con fascitis plantar, se realizó este estudio prospectivo, longitudinal, doble ciego. *Metodología*: Se incluyeron 23 participantes con fascitis plantar crónica mayores de 20 años, ya tratados con métodos convencionales. Los participantes se dividieron aleatoriamente en grupos de plasma pobre en plaquetas (PPP) y plasma rico en plaquetas (PRP). Se realizó una doble centrifugación para preparar las muestras de plaquetas y se mezclaron dos mililitros de PPP (fracción sobrenadante) o PRP (fracción de sedimento) con 1mL de solución de gluconato de calcio al 2% y se inyectaron en la fascia plantar, en dosis única. Se realizó un seguimiento a los 15 días y luego cada 60 días hasta los 180 días de aplicación y se aplicaron escalas analógicas visuales (EVA) para la evaluación del dolor y la escala de calidad de vida validada por la *American Orthopaedic Foot and Ankle Society* (AOFAS) utilizado para medir los resultados. *Resultados*: Se observó una reducción del dolor (EVA 8 para 4), en ambos grupos, en los primeros 15 días y se mantuvo hasta el 6º mes después de la aplicación de los plasmas, sin embargo, no se observó diferencia entre los grupos e también no se observó una mejora significativa en la calidad de vida de los pacientes. *Conclusión*: PPP o PRP fueron capaces de reducir la EVA, pero la presencia de plaquetas no tuvo un papel en el alivio del dolor. Otros factores en el plasma pueden desempeñar un papel en la reducción del dolor causado por la fascitis plantar durante un período de hasta 180 días.

Palabras clave: Fascite Plantar; Dolor; Plasma rico en plaquetas

1. Introduction

Plantar fasciitis is an inflammatory and degenerative condition of the proximal plantar aponeurosis of the calcaneus (Rabadi et al., 2022), in which a proliferation of fibroblasts in the inflammation site is seen. It affects more ageing and runners' population (Lopez-Lopez et al., 2021)

The most common treatment to control the inflammation is to treat it with anti-inflammatory and analgesic drugs (Lourenço et al., 2023), use dry needling for myofascial trigger points (Silva, Sousa & Rebêlo, 2022) and use orthopaedic insoles (De Souza, 2017), heels, splints and night orthotics. Physiotherapy has also been shown to reduce inflammation and pain in more than 90% of patients (Cardenuto, 2014; De Souza, 2017).

Traditional treatments have been shown to be inefficient in some cases and interventional therapies are therefore required, including corticosteroid infiltration and surgical release of the plantar fascia (Fernandes, Pedrinelli & Hernandez, 2015). The use of corticosteroids resulted in inefficacy in the short term and alternative therapies have therefore been proposed, such as using biological treatments with platelet-rich plasma (PRP) (Sathyendra et al., 2023.).

Therapies with PRP target tissue regeneration at the cellular level and they have been used to treat various pathologies, including muscle injuries (Teixeira et al., 2018) such as epicondylitis, osteoarthritis and tendinopathies (Amin I & Gelhorn A.C, 2018). The PRP therapy procedure is very safe and its costs are low, but there are uncertainties about the best method of plasma preparation (Dohan et al, 2006), volume size, injection site, addition of adjuvants, centrifugation speed and the number of platelets required for the injections (Dohan & Choukroun, 2007; Lei, Gui. & Xiao, 2009; Macedo, 2004).

According to Costa & Santos (2016), the centrifugation speed plays a key role in the quality and quantity of platelets at the time of plasma processing (Costa & Santos, 2018)

Most studies report the importance of the platelets in the samples. However, the clinical improvement in PRP injection might not only be due to the presence of platelets, as both platelet-rich plasma (PRP) and platelet-poor plasma (PPP) showed clinical improvement in the study carried out by Malahias et al. (2019).

In this study, Malahias et al. (2019) did not describe how the PRP was prepared and according to Perez et al. (2014), using low speed and time of centrifugation play key roles in the integrity and viability of platelets, therefore, the present study aimed to propose a standardization of the PRP preparation method using low speed and double centrifugation and check if it will follow the same results found by Malahias et al (2019) about the efficacy of PRP, in comparison to a control group treated with PPP, in the treatment of plantar fasciitis through a randomized, double-blind clinical trial

2. Methodology

2.1 Study Protocol

This was a prospective and longitudinal, from January to July 2020, randomized double-blinded (patient and physician) clinical trial (Pereira A. S. et al., 2018; Estrela, C., 2018; Severino, A. J., 2018) to compare the effectiveness of PRP against PPP in patients with plantar fasciitis was carried out at the Clinical Research Center of the University Hospital at Maringá State University, Paraná State, Brazil.

The protocol was followed according to Malahias et al. (2019) with slight modifications, in which the PRP was not simultaneously injected with ultrasound guidance.

The study protocol was approved by the local Ethics Committee under the number CAAE: 23598619.8.0000.0104. Patients were invited to participate in the study and the Informed Consent Form (ICF) was read and explained in detail to them. Those who agreed and signed the ICF were subsequently submitted to consultations with the principal investigator to perform an anamnesis, samples for haematological and biochemical evaluation were collected and ultrasound imaging on the test site was performed for inclusion in the study.

Patients with plantar fasciitis who also met the following criteria were invited to participate in the protocol and were scheduled for plasma application and return visits for clinical follow-up:

(a) Inclusion criteria: Participants over 18 years old, with chronic calcaneal pain for more than 3-6 months who have already been treated with traditional therapies for plantar fasciitis and who still remained refractory to traditional treatment.

b) Exclusion criteria: Participants who had the following health issues were excluded from the study:

- Previous trauma and surgeries, as well as arthrosis of the ankle and foot joints
- Those with lower-limb deformities or restrictions of joint movement
- Carriers of neurological diseases or insensitive feet
- Active infection or any local skin alteration in which the application may lead to risk of infection

The included participants' anthropometric and sociodemographic data were collected before the procedure, such as: age, height, weight, gender, race, type of work, practice of physical activity and its intensity, comorbidities and use of continuous regular medication.

All subjects have undergone USG examination, and the thickness of the central band of the plantar fascia, its insertion into the calcaneus and the echogenicity were evaluated. The pathological fascia was determined as > 4.0 mm thickness and the degree of involvement of the degeneration. Furthermore, the anatomical point of the site where the infiltration would be performed was determined before the PRP injection differing from Malahias et al. (2019).

2.2 PRP preparation and validation of the centrifugation speed

The PRP preparation was carried out according to Perez et al. (2014) and a double centrifugation were performed. In brief, the participant's blood was collected into three tubes (5mL each) containing sodium citrate. The samples were processed immediately after the blood collection and injected into the patient within one hour of collection.

The whole blood sample processing started with a centrifugation at 100g for 15 minutes (1000 rpm) at room temperature (20°C) and then, the supernatant-containing plasma from the 3 tubes were transferred into a new empty tube and centrifuged again at 200g for 10 minutes (3000 rpm). Next, the plasma was divided into 2 fractions called Platelet Poor Plasma (PPP) and Platelet Rich Plasma (PRP).

In the PPP, 2 mL of the upper fraction of the supernatant was collected with a syringe filled with a mixture of 1 mL of calcium gluconate and 1 mL of 2% lidocaine.

In the PRP, 2 mL of the sedimented fraction was collected from the bottom of the tube after the second centrifugation with a syringe with a needle filled with a mixture of 1 mL of calcium gluconate and 1 mL of 2% lidocaine.

To ensure blinding of the plasma samples, the syringes were labelled so as not to allow visualization of the contents to be injected into the patient.

Samples of whole-blood, platelet-rich-plasma and platelet-poor plasma of each subject without calcium gluconate and lidocaine enrichment were sent to quantify total platelets resulting from the doubled centrifugation to know the exact amount of platelets injected. The entire sample-preparation procedure was performed using sterile materials inside a cleanbench class IIA safety cabinet.

2.3 Plasma infiltration procedure

The participants were randomly divided into 2 treatment groups, where half were allocated as a control group to receive only PPP (poor) plasma and the other half were allocated as the treated group and received PRP (rich) plasma. The randomization process took into consideration gender, age and weight balancing in the 2 groups, and neither the physician nor the participant knew to which group they belonged. Only the unblinded staff responsible for plasma preparation knew to which group the participants had been allocated.

Antisepsis was performed by the physician in the injection site before plasma infiltration. A continuous ultrasound-guided injection was not carried out according to described by Malahias et al (2019), but the site of the proximal insertion of the plantar fascia was previously measured with ultrasound for all patients.

After injection, all participants were allowed to walk with restrictions for one week, and after this period they could return to their usual activities. To avoid any chance of exposure to infection, they were advised to avoid humid environments, as well as swimming pools and lakes. The participants were also advised not to take non-steroidal anti-inflammatory drugs or corticoids during the treatment, and that if they needed to take any new medications, they should contact their physician before starting treatment with them.

2.4 Follow-up of the clinical outcome after PRP or PPP application

The participants were evaluated using the questionnaire created by the *American Orthopedic Foot and Ankle Society* (AOFAS) (Rodrigues RC et al, 2008) to assess whether there was improvement due to the treatment. The evaluation was carried out according to the following sequence: AOFAS1: pre-treatment; AOFAS3: 60 days after application; AOFAS4: 120 days after application and AOFAS5: 180 days after application. As a complement to the pain assessment criteria, the visual analogic pain score - VAS was also employed according to the following sequence: VAS1: before treatment; VAS2:

15 days after application; VAS3: 60 days after application; VAS4: 120 days after application and VAS5: 180 days after application.

2.5 Statistical analysis

The sample size was calculated using the software G*Power (Version 3.1.9.6) (Faul et al, 2007) considering ANOVA one-way, repeated measures, within factors, 2 groups and 3 measures based on the previous study carried out by Malahias et al, 2019, which reported pain improvement in the VAS score after PRP injection was of 40%, therefore the effect size f of 0.4, power of 80% and 5% significance, which resulted in a total sample size of 20 subjects.

A descriptive analysis of the participants' clinical, anthropometric and sociodemographic data was carried out using JAMOVI® software The Jamovi Project (2021).

The variance in the VAS and AOFAS scores of the two groups at different times were tested for homogeneity using the Kolmogorov-Smirnoff test before submitting the data to parametric or non-parametric analysis. The comparison of anthropometric data was carried out by parametric analysis using a one-way ANOVA for two groups (PPP/PRP) with different characteristics. The comparison of effectiveness between the two treatment groups was carried out using a ANOVA one-way comparing the two groups (PPP/PRP) at the 3 times that the two indirect markers of VAS or AOFAS scores were collected, using JAMOVI® software, with statistical significance established at $p < 0.05$ and a 95% confidence interval.

3. Results

The initial clinical characteristics of the participants included in the study are presented in Table 1. The subjects were randomly divided into two groups: 12 in the control group (PPP) and 11 in the treated group (PRP).

Table 1 - Anthropometric, social and clinical characteristics of patients treated with platelet plasmas.

Characteristics	Platelet-Poor Plasma Mean (SD)	Platelet-Rich Plasma Mean (SD)
Gender – Female (%)	9 (75)	7 (63.64)
Age (years)	50.58 (6.83)	46.73 (12.45)
Height (cm)	1.61 (0.06)	1.68 (0.11)
Weight (kg)	85.83 (4.77)	82.55 (15.04)
BMI ^a	32.99 (6.58)	28.81 (2.70)
Compromised Foot – N(%)		
Right	4 (36.67)	2 (18.18)
Left	5 (45.83)	5 (45.45)
Both	3 (27.50)	4 (36.36)
Lifestyle - N (%)		
Smoker	2 (16.67)	1 (9.09)
Alcohol consumption	7 (58.33)	6 (54.55)
Physical activity	9 (75.00)	9 (81.82)
Comorbidades - N (%)		
Hypertension	6 (50.00)	3 (27.27)
Diabetes	2 (16.67)	0 (0.00)
Other	5 (41.67)	1 (9.09)
Drug consumption - N (%)	8 (66.67)	4 (36.36)
Initial Platelet Count (μL)	257,000 (80,00)	223,000(46,00)
Final Platelet count (μL)^b	40,297 (16,37)	579,000 (153,826)

^aBMI = Body Mass Index ; ^b After Double centrifugation. Source: Authors.

The study population contained participants from both genders, with a higher frequency of females (69.5%, n=16).

The randomization process took age and sex into consideration, but there were slight differences in age and BMI between the groups, with the PRP group being younger (46.73 vs 50.58 years) and having a lower BMI (28.81 vs 32.99) than the PPP group; however, the differences between the groups were not significant (Table 1).

With regard to comorbidities, half of the PPP group were hypertensive and 67% of them were being treated with medication. In the PRP group, only 27% of participants were hypertensive, with 36% of them taking medication.

All patients presented baseline platelet values within the normal range for inclusion in the study. The double centrifugation did not result in significantly higher concentrations of platelets in the platelet-rich samples (around 2,6 times higher) compared to the unprocessed whole-blood samples. However, the platelet counts in the platelet-poor samples were significantly lower than those in the platelet-rich and whole-blood samples.

The pain scores and quality of life scores of the patients after the application of the plasmas are described in Table 2. The baseline pain intensity measured by VAS score started at a score of 8 for both groups and in the 15-day follow up after plasma injection, a significant pain reduction was seen for both groups, reaching scores of 4 and 5 on the VAS score.

There was no significant difference in pain intensity between the groups treated with platelet-poor or platelet-rich plasma. On average, the pain score remained low in most of the patients throughout the 180-day follow-up (Table 2).

Table 2 - VAS and AOFAS scores after plasma application in patients with plantar fasciitis.

Groups Scores	Platelet-Poor Plasma Mean (DP)	Platelet-Rich Plasma Mean (DP)
VAS1	8.08 (1.08)	8.18 (1.24)
VAS2	4.92 (0.67)*	4.64 (1.36)*
VAS3	4.83 (2.48)*	4.27 (2.53)*
VAS4	4.67 (2.15)*	3.55 (3.11)*
VAS5	5.00 (2.09)*	3.27 (2.57)*
AOFAS1	66.17±7.81	69.82±9.23
AOFAS3	81.33±8.28	83.27±10.20
AOFAS4	78.64±7.57	84.45±9.90
AOFAS5	78.83±15.21	82.27±10.56

(*) p<0.05 significance level; VAS: Visual analogic pain score; AOFAS: American Orthopaedic Foot and Ankle Society. VAS and AOFAS values represent evaluation at times: 1 = before injection and 2 = 15 day, 3 = 60 days, 4 = 90 days and 5 = 180 days follow up after injection. Source: Authors

At the 60-day follow up, 50% (6/12) of the patients in the control group (PPP) presented pain scores of less than 6 compared to only 36% (4/11) in the PRP group.

The pain score remained stable after 90 and 180 days for both groups. However, 54% (6/11) of the patients treated with platelet-rich plasma presented pain scores of between 1 and 2, while only 17% (2/12) of the patients treated with platelet-poor plasma reported values between 1 and 2 after 180 days.

With regard to the patients' quality of life, measured by the AOFAS score, the baseline scores were, on average, between 64 and 66, and an improvement at the 60-day follow up was seen. Only 3 patients in each group scored below 75, and this continued up to the 90-day follow up. Among the PPP treated patients, 50% presented lower quality of life (AOFAS 60-75) and only one patient presented a score below 50% (47). In the platelet-rich group, 2 patients scored less than 60-70%, while the majority of the group scored above 80%.

In summary, independent of the presence or absence of platelets in the plasma injected into the fascia, the plasma injection by itself induced a pain reduction after 15 days, which continued up to 180 days. However, in relation to the quality-of-life score (AOFAS), no significant difference between the two groups throughout the 180 days was observed.

Despite the fact that the number of platelets present in the platelet-rich plasma samples were 10 times higher than those in the platelet-poor plasma samples, the presence of platelets did not seem to play a role in the reduction of pain or to improve the quality of life of the patients, suggesting that other components in the plasma may play a key role in pain reduction for plantar fasciitis, since several other components remained in the plasma at the centrifugation speeds used in this study.

4. Discussion

Blood plasma is rich in several endogenous substances which, at low centrifugation speeds (< 200g), remain in the plasma supernatant (Landerberg, Roy & Glickman, 2000; Pochini et al, 2016), and these substances may have played an important role in reducing the pain the patients felt after injection of plasmas with different platelet counts to treat their plantar fasciitis. This study found no difference in pain intensity due to the presence of high- or low-platelet concentrations.

The results showed that even with the application of platelet-poor plasma, pain reduction was observed at the 180-day follow up. Despite this positive effect on VAS scores, this improvement was not reflected in the quality-of-life pattern of the patients, contradicting partially the results described by Freire et al. (2020) in which the application of plasma reduced pain and improved quality of life. Other studies (Costa, Backer & Ferreira, 2014, Andia, Sanchez & Maffulli, 2010) have also observed the progressive improvement of patients' quality of life via the AOFAS score over different evaluation times.

Compared with corticosteroid infiltration (although these techniques are not currently recommended due to the risk of adverse effects (Hohmann, Tetsworth & Glatt, 2021), plasma injection maintained pain reduction for prolonged times – longer than that of the 30-day effect of the corticosteroids.

While few studies have shown the counts of platelets present in injected samples (Chahla et al, 2017), the number of platelets injected into the patients in the PRP group was about 10 times higher than that of the PPP group. However, the presence of platelets in high concentrations does not seem to be relevant, since other components are present in the plasma with autologous blood centrifugation at the speed we used. Plasma factors such as transforming growth factor-beta (TGF- β), vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) may have played a role in pain healing, stimulating tissue regeneration from mesenchymal cells acting on both cell replication and differentiation (Francheschi et al, 2014).

The lack of standardization of the PRP preparation technique may be related to the lack of efficacy described by some authors (Chahla et al, 2017). We, therefore, developed a standardized method for the preparation and infiltration of PRP. This standard protocol followed by the local institutional healthcare providers may ensure that other professionals can perform the PRP procedure in a similar manner allowing comparison between other studies.

In contrast to Perez et al.(2014), whose platelet counts remained at high concentrations even below the high speed and centrifugation time used by our group, our procedure failed to achieve platelet counts 3 to 5 times higher than the initial numbers in the whole blood samples. Because some of the older subjects included in this study had comorbidities like hypertension or diabetes, the chronic treatment with several drugs may have an impact on the blood platelets (Nusca et al, 2021; Sepulveda, Palomo & Fuentes, 2017), while Perez et al. (2014) may have used blood from healthy subjects.

The vast majority of PRP studies did not quantify platelets after centrifugation and only described clinical outcomes (Andia, Sanchez & Maffulli, 2010; Francheschi et al, 2014). Furthermore, they carried out only observational studies, where

the placebo effect may have influenced the final results since the scores used are subjective and they were not randomized or double-blinded studies.

None of the treated participants had any adverse events or complications associated with this procedure, showing that PRP/PPP injection is safe and easy to perform. Furthermore, this treatment did not require the use of sophisticated or expensive instruments, although it did require an aseptic environment for sample processing.

Our study does have several limitations: 1) the sample size was too small to show whether there is a difference in the therapeutic effect of PRP or PPP application and requires the inclusion of more participants. In order to reduce the variability among the subjects several exclusion criteria were added to reduce the sample size effect; 2) as the plantar fascia has a small area, we injected a smaller volume of PRP or PPP compared to the majority of studies carried out on other parts of the body, as there were concerns over injecting larger volumes which could reverse the benefits of the treatment, causing more harm, pain or damage to the tissue; 3) although an improvement in the pain score (VAS) after the first PRP application was observed, the results were not statistically significant in comparison to the PPP application group; 4) the study used subjective scores for comparison; however, they are the ones widely used for assessing clinical improvement; 5) the injection was applied just before the COVID-19 outbreak and some of the participants could have subsequently been quarantined at home; therefore, we asked all patients if they stayed at home or if they continued normal work routines during the 180-day follow up, and found that 4 patients, 2 from each group, had stayed at home. VAS scores were around 2-3 and AOFAS around 70 for both groups.

Compared to other studies, this study brings more details about a standardization of the PRP plasma preparation by controlling the low speed and time of centrifugation without using any diagnostic kit.

5. Conclusion

The standardization of PRP preparation achieved the same results found by Malahias related to pain reduction for up to 180 days and, regardless of whether the participants were in the PRP or PPP group. Furthermore, factors other than the platelet number are believed to have been responsible for the pain healing in the plantar fascia of the patients and more studies need to be carried out to clarify whether the platelets really have a role in the pain healing process.

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References

- Amin I. & Gellhorn A. C. (2019). Platelet-rich plasma use in musculoskeletal disorders: are the factors important in standardization well understood? *Physical Medicine And Rehabilitation Clinics Of North America*. 30(2):439-449. DOI: 10.1016/J.PMR.2018.12.005
- Andia I, Sanchez M & Maffulli N. (2010) Tendon healing and platelet-rich plasma therapies. *Expert opinion on biological therapy*. 10(10):1415-26. doi: 10.1517/14712598.2010.514603.
- Chahla J., Cinque M. E., Piuze N. S., Mannava S., Geeslin A. G., Murray I. R., Dornan G. J., Muschler G. F. & LaPrade R. F. (2017). A Call for Standardization in Platelet-Rich Plasma Preparation Protocols and Composition Reporting: A Systematic Review of the Clinical Orthopaedic Literature. *Journal of Bone and Joint Surgery*. 99(20):1769-1779. doi: 10.2106/JBJS.16.01374
- Cardenuto Ferreira R (2014). Talalgia: plantar fasciitis. *Revista Brasileira de Ortopedia*. 49(3):213-7. doi: 10.1016/j.rboe.2014.03.012.
- Costa P. A. & Santos P.(2016). Platelet rich plasma: a review of its therapeutic use. *Revista Brasileira de Análises Clínicas*.;48:311-9
- Costa M. T., Backer R. C. & Ferreira R. C. (2014). Clinical and functional evaluation of forefoot reconstruction in patients with rheumatoid arthritis. *Revista Brasileira de Ortopedia*. 49(2):167-73. doi: 10.1016/j.rboe.2014.03.020
- De Souza T. R. (2017). Eficácia do uso de palmilhas biomecânicas para a correção cinemática do padrão de pronação excessiva da articulação subtalar. *Revista brasileira de fisioterapia*.;9:275-82

- Dohan D. M., Choukroun J., Diss A., Dohan S. L., Dohan A. J., Mouhyi J. & Gogly B. (2006). Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*. 101(3):e45-50. doi: 10.1016/j.tripleo.2005.07.009
- Dohan D. M. & Choukroun J. (2007). PRP. cPRP. PRF. PRG. PRGF. FC. How to find your way in the jungle of platelet concentrates? *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, 103:305-6
- Faul F., Erdfelder E., Lang A. G. & Buchner A. (2007). G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior research methods*. 39(2): 175-91. doi: 10.3758/bf03193146
- Fernandes T. L., Pedrinelli A. & Hernandez A. J. (2015). Muscle injury - Physiopathology diagnosis, treatment and clinical presentation. *Revista Brasileira de Ortopedia*. 46(3):247-55. doi: 10.1016/S2255-4971(15)30190-7
- Franceschi F., Papalia R., Franceschetti E., Paciotti M., Maffulli N. & Denaro V. (2014). Platelet-rich plasma injections for chronic plantar fasciopathy: a systematic review. *British Medical Bulletin*. 112(1):83-95. doi: 10.1093/bmb/ldu025
- Freire M. R. M., da Silva P. M. C., Azevedo A. R., Silva D. S., da Silva R. B. B. & Cardoso J. C. (2020). Comparative Effect between Infiltration of Platelet-rich Plasma and the Use of Corticosteroids in the Treatment of Knee Osteoarthritis: A Prospective and Randomized Clinical Trial. *Revista Brasileira de Ortopedia. (Sao Paulo)*. 55(5):551-556. doi:10.1016/j.rbo.2018.01.001
- Hohmann E., Tetsworth K. & Glatt V. (2021). Platelet-Rich Plasma Versus Corticosteroids for the Treatment of Plantar Fasciitis: A Systematic Review and Meta-analysis. *The American Journal of Sports Medicine*. 49(5):1381-1393. doi: 10.1177/0363546520937293
- Jarde O., Diebold P., Havet E., Boulu G. & Vernois J. (2003). Degenerative lesions of the plantar fascia: surgical treatment by fasciectomy and excision of the heel spur. A report on 38 cases. *Acta orthopaedica Belgica*. 69(3):267-74
- Landesberg R., Roy M. & Glickman R. S. (2000). Quantification of growth factor levels using a simplified method of platelet-rich plasma gel preparation. *Journal of Oral Maxillofacial Surgery*. 58(3):297-300; discussion 300-1. doi: 10.1016/s0278-2391(00)90058-2
- Lei H, Gui L & Xiao R. (2009). The effect of anticoagulants on the quality and biological efficacy of platelet-rich plasma. *Clinical Biochemistry*. 42(13-14):1452-60. doi: 10.1016/j.clinbiochem.2009.06.012
- López-López, D., Pérez-Ríos, M., Ruano-Ravina, A., Losa-Iglesias, M. E., Becerro-de-Bengoa-Vallejo, R., Romero-Morales, C., Calvo-Lobo, C., & Navarro-Flores, E. (2021). Impact of quality of life related to foot problems: a case-control study. *Scientific reports*, 11(1), 14515. <https://doi.org/10.1038/s41598-021-93902-5>
- Lourenço, B. M., Campos, M. G. M., Maia, L., Castro, B., Trede, R. G., & Oliveira, V. C. (2023). Efficacy of pharmacological and non-pharmacological therapies on pain intensity and disability for plantar fasciitis: a systematic review and meta-analysis. *British journal of sports medicine*, bjsports-2022-106403. Advance online publication. <https://doi.org/10.1136/bjsports-2022-106403>
- Macedo A. P. (2004). Plasma Rico Em Plaquetas : Uma Análise Quantitativa e Plasma Rico em Plaquetas : Uma Análise Quantitativa E. Repositorio.Ufsc.Br repositorio.Ufsc.Br.
- Malahias M. A., Mavrogenis A. F., Nikolaou V. S., Megaloikonos P. D., Kazas S. T., Chronopoulos E. & Babis G. C. (2019). Similar effect of ultrasound-guided platelet-rich plasma versus platelet-poor plasma injections for chronic plantar fasciitis. *Foot (Edinb)*. 38:30-33. doi: 10.1016/j.foot.2018.11.003
- Nusca A., Tuccinardi D., Peralice S., Giannone S., Carpenito M., Monte L., Watanabe M., Cavallari I., Maddaloni E., Ussia G. P., Manfrini S. & Grigioni F. (2021). Platelet Effects of Anti-diabetic Therapies: New Perspectives in the Management of Patients with Diabetes and Cardiovascular Disease. *Frontiers in pharmacology*. 12:670155. doi: 10.3389/fphar.2021.670155
- Perez A. G. M., Lana J. F. S. D., Rodrigues A. A., Luzo A. C. M., Belangero W. D. & Santana M. H. A. (2014). Relevant Aspects of Centrifugation Step in the Preparation of Platelet-Rich Plasma. *ISRN Hematology*. 25:176060. DOI:10.1155/2014/176060
- Pochini A. C., Antonioli E., Bucci D. Z., Sardinha L. R., Andreoli C. V., Ferretti M., Eijnisman B., Goldberg A. C. & Cohen M. (2016). Analysis of cytokine profile and growth factors in platelet-rich plasma obtained by open systems and commercial columns. *Einstein (Sao Paulo)*. 14(3):391-397. doi: 10.1590/S1679-45082016AO3548
- Rabadi, D., Seo, S., Wong, B., Chung, D., Rai, V., & Agrawal, D. K. (2022). Immunopathogenesis, early Detection, current therapies and prevention of plantar Fasciitis: A concise review. *International immunopharmacology*, 110, 109023. <https://doi.org/10.1016/j.intimp.2022.109023>
- Rodrigues, R. C., Masiero, D., Mizusaki, J. M., Imoto, A. M., Peccin, M. S., Cohen, M., & Alloza, J. F. M.. (2008). Tradução, adaptação cultural e validação do "American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale". *Acta Ortopédica Brasileira*, 16(2), 107-111. <https://doi.org/10.1590/S1413-78522008000200009>
- Sathyendra, K. G., Dnyandeo Solankey, R., Singh, M., Venkatesh Kumar, S., Singh, G., & Gupta, M. M. (2023). Comparative study of local injections of autologous platelet rich plasma versus corticosteroid in management of chronic plantar fasciitis. *Journal of clinical orthopaedics and trauma*, 43, 102225. <https://doi.org/10.1016/j.jcot.2023.102225>
- Sepúlveda C., Palomo I. & Fuentes E. (2017). Antiplatelet activity of drugs used in hypertension, dyslipidemia and diabetes: Additional benefit in cardiovascular diseases prevention. *Vascular Pharmacology*. 91:10-17. doi: 10.1016/j.vph.2017.03.004
- Silva, R. D. O.; Sousa, G.A.; Rebêlo, V.C.N. (2022). Dry neeling method and its effectiveness in the treatment of Plantar fasciitis: review of the literature of randomized clinical trials. **Research, Society and Development**. [S. l.], v.11, n.5, p. e31311528416. DOI: 10.33448/rsd-v11i5.28416.
- Teixeira M. V. T. Takamori E. R. Menezes K. Carias R. B. V. & Borojevic R. (2018). Utilização de plaquetas e de produtos derivados de plaquetas humanas em terapias avançadas. *Vigilância Sanitária em Debate*;28;6:125
- The Jamovi Project (2021). *Jamovi* (Version 1.6) [Computer Software]. Retrieved from <https://www.jamovi.org>