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Systematic Review

The use of Platelet Rich Plasma in the Management of Plantar Fasciitis: A Systematic Review

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Plantar fasciitis is the most common cause of heel pain, highly prevalent in orthopedic practices. The present study aims to investigate current evidence on Platelet-Rich Plasma on plantar fasciitis treatment, comparing biologic intervention with other minimally invasive options. Despite a lack of standardization regarding process, delivery methods and specific indications of treatment, short and long term benefits have been demonstrated.To realize such investigation, this article has basis in researching some scientific publications that discuss the effectiveness of platelet-rich plasma therapy. And its short, medium and long-term results when compared with other minimally invasive treatments modalities. As an important outcome, there was a significant clinical improvement, effective and lasting for patients between 6 and 12 months after implementing platelet-rich therapy. Although, like mentioned above, a lack of standardization regarding obtention, processing, and delivery of such therapy is yet an issue.

Keywords: Plantar fasciitis, heel pain, platelet-rich plasma

INTRODUCTION

Plantar fasciitis (PF) is the most common cause of heel pain. Approximately 10% of the population develops the condition throughout life. The main symptoms are morning pain and pain at the beginning of activities (after resting time). Pain is felt near the medial and proximal insertion of the plantar fascia in the calcaneus tuberosity, or, less commonly, under heel pad, which leads to dysfunction and limitation for recreational and work activities (Zhiyun et al., 2013; Riddle et al., 2003).

The etiology of PF is not yet clearly defined, but several risk factors such as bone spurs, flat feet, obesity, diabetes, rheumatic disorders, lower limb length discrepancy, improper footwear, long time in orthostasis and runner athletes have been considered as part of such risks (Zhiyun et al., 2013; Mohseni-Bandpei et al., 2014).

PF diagnosis is clinical, based on pain site, morning symptoms and worsening with use of low heeled

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shoes. Radiography, ultrasound or magnetic resonance images (MRI) are considered confirmatory tools if clinical diagnosis is not clear, or to rule out other common causes of heel pain, such as calcaneus stress fractures and Baxter neuropathy (Schwartz, 2014; Sign et al., 2017).

Radiographically, the calcaneal spur can be seen in foot profile images in approximately 50% of patients with pain, but the correlation between that and patient's clinical condition is still uncertain. (Mohseni-Bandpei et al., 2014)

It is largely accepted that the primary treatment is conservative, often presenting good results. Conservatives modalities include home stretching program, prescription of insoles and orthotics to shock wave therapy. Interventional therapies include corticosteroid infiltration, surgical release of the plantar fascia and, more recently, biological therapies such as platelet-rich plasma (PRP) (Mohseni-Bandpei et al., 2014).

This article aims to evaluate current evidence on PRP for the management of chronic refractory plantar fasciitis, its indications, obtaining processes and delivery methods.

METHODOLOGY

The terms *platelet-rich plasma, platelet rich-plasma, plantar fasciitis and plantar fascitis* were used to search in Medline (PubMed), Lilacs (Bireme). As a result, we found 53 and 43 articles with the above-mentioned terms, respectively, totaling 98 articles with publication until July 2018.

RESULTS

After filtering for "Orthopedics and Traumatology" and / or "Sports Medicine", we excluded 14 articles. Next, we applied a new searching filter to find out which articles had a human research approach, resulting in a total of 72 articles. Out of those 72, 6 were not written in the English language and were not considered for this article.

As the present study seeks the analysis of interventional techniques, only clinical trials were selected, leaving a total of 35 articles. After careful reading the titles and abstracts of such papers, we realized that some of them had similar content. Also, some others were not included because it was not pertaining to the objective of the present study. After filtering the initial 98 publications, 12 were the publications selected for analysis (Figure 1).

Two reviewers independently evaluated the methodological quality of the trials included, using a12-item scale. The weighted kappa of agreement in the analysis of the quality of the clinical trial among the reviewers was 0.94 (95% with a confidence interval of 0.78-0.99).

The following characteristics were analyzed and highlighted: sample size, PRP application rates, methods used, evaluated scores, and follow-up time of the patients. As a criterion of inclusion in the study, we also analyzed individuals diagnosed with chronic PF and receiving treatment with PRP (Table 1 below).

In Mahindra's studies (2016), seventy-five patients were analyzed, comparing the effect of PRP, corticosteroid (methylprednisolone) and placebo. In the PRP group, the material was obtained by collected27 ml of blood from the ulnar vein and placing the blood in a glass tube containing an anticoagulant. Blood was centrifuged at 3200 rpm for 12 min and 2.5 to 3 ml of PRP was obtained. In the corticoid group, 2mL / 40mg of methylprednisolone was used and in the placebo group, saline infiltration was performed. Infiltrations were made at multiple sites of the plantar fascia. Patients were evaluated before infiltration, three weeks and three months using American Orthopedic Foot and Ankle Society (AOFAS) and Visual Analogue Score (VAS) scores.

It was observed that in the three months following the infiltrations, that according to the visual analog scale and to AOFAS score, the placebo group did not show improvement. Meanwhile, groups that received infiltration did show improvement, having a significant improvement in symptoms. However, it was not possible to determine the superiority of PRP or corticoid.

Jain et al. (2015) analyzed sixty feet of a total of forty-six patients who had PF symptoms for at least twelve months, comparing the effect of PRP and corticosteroid. To obtain PRP, 27 ml of blood was collected from peripherical blood and 3 ml of sodium citrate was added as an anticoagulant. The mixture was centrifuged for 15 minutes at 3200 rpm. As a result, 2.5 ml of platelet-rich plasma was obtained. Infiltrations were performed in the area of greater sensitivity of the plantar fascia. Patients were assessed before, and three, six and twelve months, using Roles-Maudsley (RM), VAS and AOFAS scores.

After three months, the three scores obtained improved significantly from their pre-treatment level in both groups. The scores in the steroid group were better than in the PRP group, but the difference was not statistically significant. After six months, there was no statistically significant difference between the two groups, although there was a tendency for PRP scores to be better than the steroid group scores. After twelve months, the scores in the PRP group were significantly better than the steroid group.

Say et al. (2014) analyzed fifty patients with PF symptoms for at least three months, comparing the effect of PRP and corticoid (methylprednisolone) associated with a local anesthetic (prilocaine). To obtain the PRP, 30 ml of blood was collected from peripherical blood and

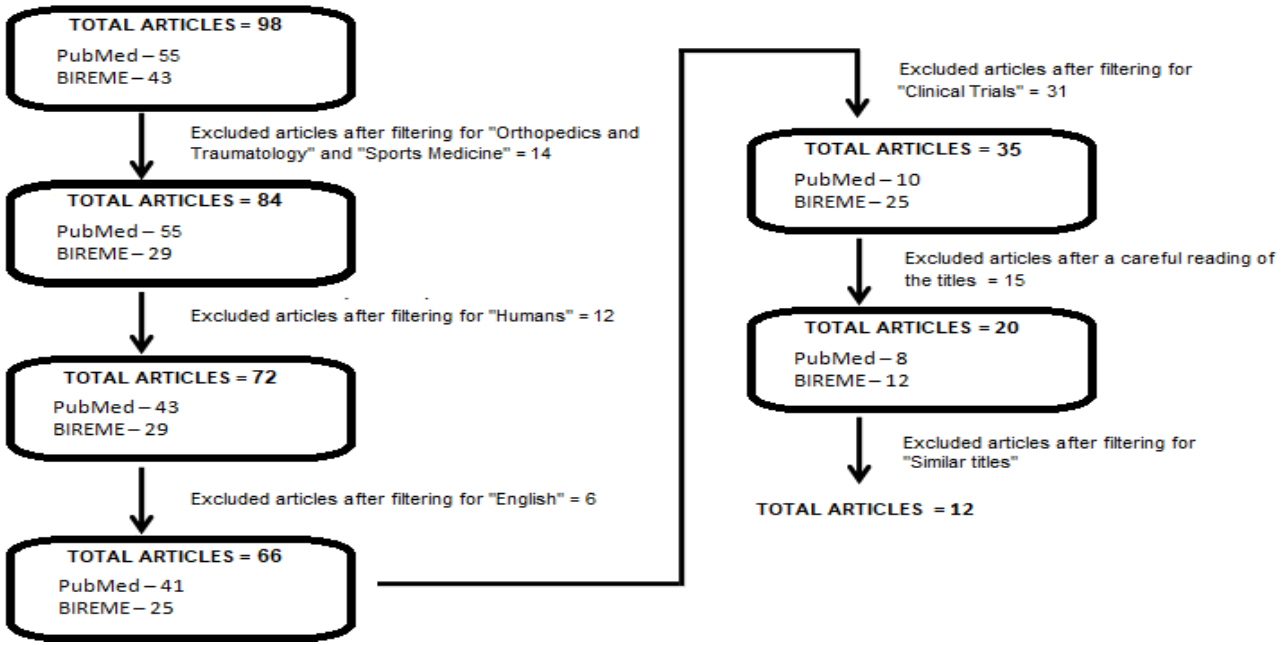

Figure 1. Demonstration of studies selection process

Table 1. Platelet rich plasma studies in the treatment of chronic plantar fasciitis

Publication	Patients	Comparison Methods	PRP Dosage	Scores	Evaluation Time	Conclusion
Mahindra et al. 2016	75	Placebo, Methylprednisolone and PRP	1	AOFAS VAS	Before the procedure, 3 weeks and 3 months	Not possible to determine the superiority of PRP or corticoid
Jain et al. 2015	46 (60 feet)	PRP e Cortisone	1	RM VAS AOFAS	Before the procedure, 3, 6 and 12 months	PRP is more effective than long-term corticoid
Say et al. 2014	50	PRP and Methylpredinisolone + prilocaine	1	VAS AOFAS	Before the procedure, 6 weeks and 6 months	Betterresultswith PRP
Shetty et al. 2014	60	PRP and Triamcinolone + lidocaine	1	VAS AOFAS FADI	Beforethe procedure, 3 months	Betterresultswith PRP
Monto 2014	40	PRP and Methylpredinisologin	1	AOFAS	Before the procedure, 3, 6, 12 and 24 months	PRP is more effective than long-term corticoid

Kim 2014	21	PRP and Prolotherapy (dextrose + lidocaine)	2 (0 e 2 weeks)	FFI	Before the procedure, 2 and 6 months	No difference was observed between methods. However, PRP has demonstrated efficacy in the disability limitation subscales
Martinelli et al. 2012	14	There was no comparison of methods	3 (0, 7 and 14 days)	RM VAS	Before the procedure and 12 months	PRP is safe and effective
Gogna et al. 2016	40	PRP e LDR	1 *LDR 3Gy (0,5Gy 2x/weeks)	USG AOFAS VAS	Before the procedure, 3 and 6 months	PRP more effective in the short term. No long-term differences.
Kumar et al. 2013	44 (50 feet)	There was no comparison of methods	1	RM AOFAS VAS	Before the procedure, 3 and 6 months	PRP is safe and effective
Ragab 2012	25	There was no comparison of methods	1	VAS USG	Before the procedure, 2 weeks, 3 and 6 months and one year	PRP is safe and effective
Aksahin et al. 2012	60	PRP and Methylprednisolone + lidocaine	1	RM modified VAS	Before the procedure, 3 weeks and 6 months	Effective methods, without significant difference
Wilson et al . 2013	22 (24 feet)	There was no comparison of methods	1	FAM and Foot-SANE	Before the procedure, 4, 8, 12, 16, 32 and 52 weeks	PRP is safe and effective

PRP = Platelet rich plasma
AOFAS = American Orthopedic Foot and Ankle Society
VAS = Visual Analogue Score
RM = Roles-Maudsley
FADI = Foot & Ankle Disability Index
FFI = Foot Function Index
FAM = Ankle Ability Measure
Foot-SANE = Foot Single Assessment Numeric Evaluation

sodium citrate was added. The mixture was centrifuged for 8 minutes at 1800 rpm and 3.5 ml of platelet-rich plasma were obtained, but only 2.5 ml were useful. In the corticoid group, 1 ml / 40mg of methylprednisolone was used, associated with 1 ml of prilocaine. Infiltrations were performed in the region of greatest sensitivity of plantar fascia. Patients were assessed before, at six weeks and six months using VAS and AOFAS scores.

In Say et al. (2014) it was concluded that the PRP group presented better results in the AOFAS and VAS scores, with statistical significance when compared to the corticoid group.

Schetty et al. (2014) analyzed sixty patients that presented PF symptoms for at least three months, comparing the effect of PRP and corticoid (triamcinolone) associated with a local anesthetic (lidocaine). To obtain the PRP, 54 ml of blood was collected from peripherical blood and 6 ml of sodium citrate was added, this mixture was centrifuged for 14 minutes (centrifugation rate was not reported in the study) and 10 ml of platelet-rich plasma was obtained. In the corticoid group, 40mg of triamcinolone was used, associated with 3 ml of 2% lidocaine. The infiltrations were performed in the area of greater sensitivity of the plantar fascia. The patients were evaluated before infiltration and three months, using VAS, AOFAS and Foot and Ankle Disability Index (FADI) scores.

It was observed a significant difference in both groups for all postoperative scores, with better results in the PRP group compared to the corticosteroids group.

Monto (2014) analyzed forty patients with four months of PF symptomatology comparing the

effect of PRP and corticoid (methylprednisolone). To obtain the PRP, 27 ml of blood was collected from peripherical blood and 3 ml of sodium citrate was added. The mixture was centrifuged for 12 minutes at 2400 rpm, 3 ml of PRP being obtained. In the corticoid group, 40mg of methylprednisolone was used. The infiltrations were performed in the area of greater sensitivity of the plantar fascia. The patients were evaluated before, three, six, twelve and twenty-four weeks, using AOFAS score.

Monto study demonstrated that use of PRP in a long-term was more effective than the traditional cortisone injection treatment and appears to be safer than the current surgical alternatives.

Kim (2014) analyzed twenty-one patients diagnosed after ultrasonography and presenting PF symptoms for at least six months. It was compared the effect of PRP and dextrose prolotherapy associated with lidocaine. To obtain PRP, 20 ml of blood was collectedfrom the antecubital vein and 2 ml of sodium citrate was added. The material was centrifuged for 3 minutes at 3200 rpm, 2 ml of platelet-rich plasma being obtained. In the dextrose group, 1.5 ml of 20% dextrose associated with 0.5 ml of 0.5% lidocaine resulted in a 15% dextrose solution. The infiltrations were performed guided by ultrasonography and applied in abnormal hypoechoic areas. The patients were submitted to two doses of infiltrations in the plantar fascia, one at "zero time" and another two weeks after, and the Foot Function Index (FFI) score was applied at the time of pre-injection, two and six months after infiltration.

No significant statistical difference was observed in any follow-up. In subcategories of pain and disability, both presented substantial improvement. PRP demonstrated efficacy in the disability and limitation subscales.

Martinelli et al. (2012) analyzed fourteen patients with six months of PF symptoms and radiographic diagnosis of the plantar spur. The study evaluated PRP injections safety to treat chronic PF and provide an initial clinical evaluation of its efficacy, without comparison of methods. To obtain the PRP, 10 ml of blood was collected from the antecubital vein and 2 ml of dextrose citrate was added. The blood was placed in the centrifuge for 5 minutes at 1500 rpm, 5 ml of platelet-rich plasma was obtained. Infiltrations were performed medially to the calcaneal tubercle at the origin of the plantar fascia. Patients underwent three doses of infiltration into the plantar fascia, one at "zero time", the second at seven days and the third dose at fourteen days after the first injection. VAS and MRI scores were applied before and after one year of the first infiltration.

No systemic or local complications were observed at any time. At the end of the cycle, the fourteen patients reported improvement in pain and function. Both of the analyzed scores showed a significant improvement proving that PRP is safe and effective for chronic PF treatment.

Gogna et al. (2016) analyzed fourteen patients with PF symptoms for at least six months comparing the effect of PRP with a low dose radiation therapy (LDR). To obtain the PRP, 20 ml of blood was taken from the patient and processed according to the GPS System Instruction protocol (without a description of the method of obtaining PRP), and 3 ml of platelet-rich plasma was obtained. In the LDR group, a total radiation of 3.0 Gy was administered at doses of 0.5 Gy twice weekly. Infiltrations and applications were performed guided by ultrasonography in the area of greater thickening of the plantar fascia. Patients were evaluated before, three and six months, using AOFAS, VAS scores and plantar fascia thickening visualized by ultrasonography.

The study clarified that the PRP use was equivalent when compared to long-term low-dose radiation therapy for PF chronic treatment. However, the PRP group has been shown to be more effective in the short term. The author concluded that PRP has a discreet advantage over LDR due to the need for fewer interventions and access to the method more easily.

Kumar et al. (2013) analyzed fifty feet of forty patients, with symptoms of PF with at least one year of evolution and refractory to conservative treatment. In the study, it was evaluated the efficiency of PRP injections to treat chronic PF, without comparison between methods. To obtain PRP, 27 ml of blood was collected from peripherical blood and 3 ml of citrated sodium citrate were added and centrifuged for 15 minutes at 3200 rpm, with 2.5 to 3.5 ml of platelet-rich plasma being obtained. Infiltrations were performed in the area of greatest pain in the FP region and patients were then instructed to maintain a stretching program together. The patients were evaluated before, three and six months according to MR, AOFAS, VAS scores.In that study, good PRP efficacy was observed for chronic PF treatment, showing a good safety of use method, since no complications were observed.

Ragab (2012) analyzed twenty-five patients, with symptoms of PF for at least six months, without comparison between methods. To obtain the PRP, 50 ml of blood was collected from peripherical blood and 5 ml of sodium citrate was added. Following a protocol, the mixture was centrifuged for 15 minutes at 3000 rpm, and between 5 ml of platelet-rich plasma was obtained. The infiltrations were performed in the area of greatest pain in the plantar fascia region. Patients were evaluated before, two weeks, three months, six months and one year by VAS score and ultrasound measurements of the plantar fascia.Here it was evidenced that the use of PRP is safe and does not affect the biomechanical function of the foot and, therefore, is a good method to treat this pathology.

Aksahin et al. (2012) analyzed sixty patients with symptoms of PF for at least three months, comparing the effect of PRP and corticoid (methylprednisolone) associated with a local anesthetic (lidocaine). To obtain

PRP, 25 ml of blood was taken from the patient and calcium citrate was added. After application to the centrifuge for 15 minutes at 1800 rpm for erythrocyte separation and then further centrifugation of 10 minutes at 3500 rpm, resulting in 3 ml of platelet-rich plasma. In the corticoid group, 2 ml / 40 mg of methylprednisolone was used associated with 2 ml of 2% lidocaine. Infiltrations were performed in the area of greater sensitivity of the plantar fascia. Patients were assessed before, three weeks and six months according to the modified MR and VAS scores. The study demonstrated no significant difference between the methods, proving that both are effective and present good results in the treatment of plantar fasciitis. However, PRP seems to be a safer method.

Wilson et al (2013) analyzed twenty-four feet of twenty-two patients with symptoms of PF for 3 months. No comparison of methods. To obtain the PRP, 45 ml of blood was collected from peripherical blood and added to an already anticoagulant syringe (dextrose citrate), and 5 ml of platelet-rich plasma was obtained. The infiltrations were performed in the area of greater pain in the plantar fascia region and greater thickening in ultrasound evaluation. Patients were assessed before, four weeks, eight weeks, twelve weeks, sixteen weeks, thirty-two weeks, and fifty-two weeks, using the Foot and Ankle Ability Measure (FAM) and Foot Assessment (SANE).

In Wilson et al (2013)was demonstrated that the use of PRP had subjective improvement of the patient's pain without significant side effects, and is an alternative safe method when compared to the use ofcorticosteroids or to surgical treatment.

DISCUSSION

The twelve studies analyzed by this article evaluated patients with chronic plantar fasciitis with months of out follow-up and refractory results to a conservative treatment.

Martinelli et al. (2012), Kumar et al. (2013), Ragab (2012) and Wilson et al. (2013) carried out their analysis without comparison between methods, using PRP at the most painful point of the plantar fascia. However, Wilson et al (2013) used USG guided infiltration. The authors who evaluated PRP only as a treatment for plantar fasciitis demonstrated that the method can be considered effective and safe, using several scores for evaluation.

A point of greatest sensitivity of the plantar fascia was chosen by the authors to apply all method. Kim (2014), Gogna et al. (2016) and Wilson et al. (2013) performed the procedure guided by an ultrasound device.

As per dosage, most studies used a single dose for treatment. However, Kim (2014) presented applications in two distinct times, one at "time zero" and another two weeks after the first infiltration. Martinelli et al. (2012) also worked with more than one dosage, with three infiltrations, one at "zero time", another at 7 days, and the last after 14 days. These studies did not demonstrate better end-results when compared to the single dose.

Gogna et al. (2016) evaluated the comparison between low dose radiation therapy and PRP, demonstrating that PRP is more effective in the short term, but without long term differences. Monto (2014) and Jain et al. (2015) evaluated the comparison between PRP and corticosteroid, demonstrating that PRP was a better option when compared to the comparative method in the long-term evaluation.

There was a disagreement between the authors regarding the best time for scores application and the total time of patients' final follow-up. VAS, AOFAS and RM were the most used scores.

Most studies demonstrate long-term clinical improvement of patients using PRP. It is believed that PRP therapy should be evaluated as a promising and effective method for chronic plantar fasciitis treatment.

CONCLUSION

This article demonstrated that the use of PRP therapy is effective and safe when compared to current different methods used for PF chronic treatment, presenting better clinical results in the medium and long-term. Despite that fact, it was also demonstrated that there was no consensus among the authors regarding the ideal time to perform the treatment, as well as an ideal dose and the best method to obtain PRP.

Therefore, new studies must be carried out for standardization of obtaining, processing, infiltration, as well as to elucidate the clinical scenario in which using PRP is most advantageous. It is necessary to seek customization of the PRP at the individual level, referring to the volume, platelet concentration, activation methods and other variables, given the clinical situation of each patient.

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