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A Comparison between the Effectiveness of Platelet-Rich Plasma Injection and Corticosteroid Injection in Plantar Fasciitis Patients: A Systematic Review

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Abstract

A systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses chart (PRISMA) was used in this study. About 7 articles have been included. A month post-injection, corticosteroid injection reduced pain more than PRP injection (Mean: 1.22; 95% CI:-1.10 to 3.54; p=0.30).However, PRP injection reduced pain significantly more than corticosteroid injection in three months after injection (Mean: -0.77, 95% CI:-1.46 to -0.96; p=0.03), and in six months later (Mean:-1.22, 95% CI:-2.02 to -0.42; p=0.003). The effectiveness difference between Platelet-Rich Plasma injection and corticosteroid injection in patients with plantar fasciitis varies depending on peak period and facial thickness.

Keywords: Plantar fasciitis; Corticosteroid injection; Platelet-rich plasma Injection; Systematic review; Effectiveness.

Introduction

Plantar fasciitis is a disease characterized by inflammation of the plantar fascia. Patients with *plantar fasciitis* usually feel non-spread pain that feels stabbing.[1] The pain worsens when patients begin to stand up after resting, and the symptom will primarily come in the morning. The pain gradually decreases in line with the use of the foot in activities, although it does not completely heal. Pain can be worsened if the patient stands or walks for too long, does strenuous activities, or lifts heavyweights for a long time.[2]

The leading cause of plantar fasciitis is still undetected in specific ways.[3] However, some researchers believe that one of the causes is the formation of small tears in the plantar fascia, which repeatedly cause inflammation. Factors related to these tears include obesity, excessive running, a sedentary lifestyle, the shape of the foot is too flat (pes planus), the foot angle is too high (pes cavus), or work that requires walking or standing for a long duration.[4]

Plantar fasciitis has a self-limiting character;

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hence, the rigid standard of the therapy has not been defined yet.[5] Several therapeutic modalities, such as administering non-steroidal anti-inflammatory drugs, stretching, orthotics, and shock waves, can accelerate healing and improve the patient's quality of life, aiming those patients to carry out normal daily activities.[6] When these noninvasive modalities are unsuccessful, injections of drugs such as corticosteroids can be performed.

Corticosteroids are one of the most effective drugs to treat inflammation. The strong anti-inflammatory effect of corticosteroids can help heal the inflammation quickly, although it can cause some side effects and complications.[7] Despite being considered an effective treatment in reducing pain, the side effects and complications have led many researchers to look into alternative drugs, which are more effective and efficient for managing plantar fasciitis.[8]

Platelet-Rich Plasma (PRP) has become another safer alternative compared to corticosteroid injection for curing plantar fasciitis.[9] PRP therapy has recently become famous for the healing of various tissues in various medical fields. PRP is a biological product taken from the patient himself in plasma, which has a platelet concentration above the average.[10] It can release growth factors and cytokines that are useful in the healing process. Because of that, the effectiveness for specific tissues, which have low healing potentials such as tendons, ligaments, fascia, and plantar fascia, has been proven (Wu, Diaz, and Borg-Stein, 2016). The concept of PRP, which is taken from the patient itself, can minimize the possibility of rejection reactions, side effects, and complications. Hence, this theory has made PRP a safer alternative compared to corticosteroids.[8] However, many practitioners are still debating whether PRP injections are more effective in treating plantar fasciitis than corticosteroid injections.[11]

The purpose of this study was to systematically analyze the comparison of the therapeutic effectiveness of Platelet-Rich Plasma injection when compared to corticosteroid injections in treating patients with plantar fasciitis.

Methods

A systematic review using a meta-analysis approach was used in this study. The results of the primary studies were synthesized using a statistical (quantitative) approach. The journal search protocol was adjusted to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses chart (PRISMA). Collecting articles was conducted using the PubMed and ScienceDirect databases by applying several keywords: 'Platelet-Rich Plasma' or 'Corticosteroids', and combined with 'Plantar fasciitis'. The selected period was the last ten years, namely from 2010 to 2020.

Quality and bias assessment was carried out using the COCHRANE Risk of Bias Tools which was used to assess bias in research using the RCT (Randomized Controlled Trial) method.[12] The risk of bias was assessed in 5 areas: the randomization process, deviations from predetermined interventions, missing data output, measuring output, and reporting results.[13]

The population was primary research data on Plantar fasciitis patients who have undergone Platelet-Rich Plasma (PRP) injection or corticosteroid injections and published in the PubMed and ScienceDirect databases. The samples were research journals that met the inclusion criteria: reporting differences between Platelet-Rich Plasma (PRP) injections and corticosteroid injections in Plantar fasciitis patients; using the RCT (Randomized Controlled Trial) method; using the Visual Analog Scale (VAS) pain measurement instrument; in a maximum period of 10 years, evaluating post-injection therapy after 1, 3 or 6 months; the most recent and most complete studies. Meanwhile, the exclusion criteria used include: Studies without good method validation; Studies are not written in Indonesian or English; Studies with a period longer than the last ten years, in poor condition, and incomplete.

The instrument used was a search database for research journals, namely PubMed and ScienceDirect, which are used to search for research journals with predetermined topics. COCHRANE Risk of Bias Tools Version 2 (RoB 2) was also used to conduct a biased assessment on the journal to be used. To perform quantitative analysis, COCHRANE Review Manager (RevMan) version 5.4 was used.

Results

According to the accumulated articles, as many as 1534 journal articles were founded on the database. To obtain appropriate articles, multiple screening was done by using several predetermined criteria, such as duplication, the specified time span of 10 years, the Randomized Controlled Trial

(RCT) method, language used, the use of Visual Analog Scale in measuring pain, the duration of out post-therapy evaluation. There were 17 articles indicated duplication, 37 articles provided short-text and without abstract; 617 articles exceeded from the length of 10 years period; 785 articles without using Randomized Controlled Trial (RCT) method; 2 articles iliminated as they donnot write in English or Indonesia; 65 articles were out of topic discussed; and 2 articles were not using Visual Analog Scale.Finally, about seven journal articles have been included in a systematic review for extraction and analysis, thereby drawing conclusions from the journal data.

The risk assessment results of bias in the seven journals used can be seen in Figures 1, which state that the risk of bias is relatively small. Several areas have a high risk due to lack of information in journals about the related area.

Articles Description

The research design in each study was carried out in parallel in each group. All studies used patients with plantar fasciitis who failed conservative treatment for at least three months and had never had surgery.

The total sample of all studies used was 497, which varied from 25 samples to 60 samples in each group. All studies used clinical features and physical examination to diagnose Plantar fasciitis in each sample used. Four studies (Jain, Khurana, Sherpy and Uğurlar)[7,9,11,14] performed further imaging using either ultrasonography or MRI to confirm a further diagnosis of Plantar fasciitis. Each group in the study received one injection each in both the PRP and corticosteroid injection groups, except in the study by Uğurlar, which gave three injection sessions seven days apart for each injection.Apart from 2 studies (Khurana and Uğurlar)[9,14], all studies included patients in a post-injection stretching exercise program.

Pain Felt a Month Post-Injection

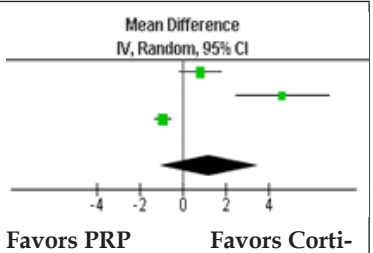
Meta-analysis and Forest Plot showed that a month post-injection, corticosteroid injection reduced pain more than PRP injection, but it was not significantly (Weighted Mean Difference: 1.22; 95% CI: -1.10 to 3.54; p= 0.30). The heterogeneity of the studies was assessed as the highest (Chi2=33.01; I2=94%), which may be due to the small number of studies used in a month post-injection analysis. Besides, the study by Uğurlar used a different route of administration of the injection (Table 1).

Pain Appeared3 Months Post-Injection

Of the seven studies selected for analysis, six studies had pain measurement data 3 months post-injection, as can be seen in Table 2. Meta-analysis and Forest Plot showed that PRP injection reduced pain significantly more than corticosteroid injection (WMD: -0.77, 95% CI: -1.46 to -0.96; p=0.03). Heterogeneity in the study was considered quite high (Chi^2=15.63; I^2=68%).

Table 1. Meta-analysis evaluation of pain measurement one month after injection using a visual analogue scale (VAS).

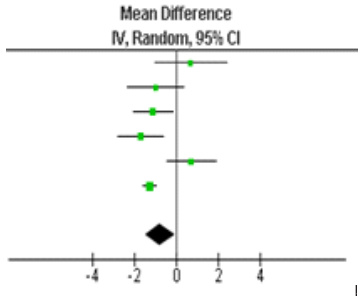
Study of subgroup	PRP injection		Corticosteroid Injection		Weight	Mean Difference IV, Random 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Mean	SD			
Jain et al, 2018	6.5	1.7	5.7	2.7	34.9%	0.80 [-0.19, 1.79]	
Ugurlar et al, 2018	7.8	6.5	3.2	2.4	28.1%	4.60 [2.43,6.77]	
Khurana et al, 2020	3.98	1.03	4.93	1.07	36.9%	-0.95 [-1.33, -0.57]	
Total (95% CI)					**100%**	**1.22 [-1.10, 3.54]**	



Heterogeneity: Tau^2= 3.75; Chi^2= 33.01, df=2(P<0.00001) I^2= 94%
Test for overall effect Z=1.03(P=0.30)

Figure 2: Meta-analysis evaluation of pain measurement 3 months after injection using a visual analog scale (VAS)

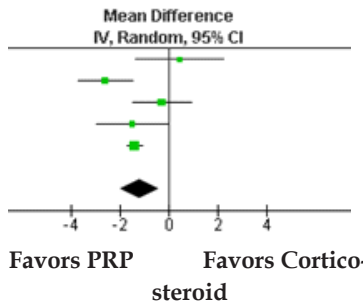
Study of subgroup	PRP injection		Corticosteroid Injection		Weight	Mean Difference IV, Random 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Mean	SD			
Jain et al., 2015	3.5	3.3	2.83	3.44	10.2%	0.67 [-1.04, 2.38]	
Sherpy et al., 2015	0	2.5	1	2.25	13.7%	-1.00 [-2.32,0.32]	
Mahindra etal.,2016	2.52	1.71	3.64	1.62	18.4%	-1.12 [-2.04, -0.20]	
Jain et al, 2018	5	2.5	4.3	2.8	15.4%	0.70 [-0.46, 1.86]	
Ugurlar et al, 2018	2.7	0.3	4.4	3.5	16.3%	-1.70 [2.79, -0.61]	
Khurana et al, 2020	1.45	0.75	2.72	0.98	26%	-1.27 [-1.58, -0.96]	
Total (95% CI)					**100%**	**-0.77 [-1.46, -0.08]**	



Heterogeneity: Tau²= 0.45; Chi²= 15.63, df=5 (P=0.008) I²= 68%
Test for overall effect Z=2.20 (P=0.03)

Table 3: Meta-analysis evaluation of pain measurement 6 months after injection using a visual analogue scale (VAS).

Study of subgroup	PRP injection		Corticosteroid Injection		Weight	Mean Difference IV, Random 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Mean	SD			
Jain et al., 2015	3.7	3.58	3.28	3.55	12.4%	0.42 [-1.38, 2.22]	
Ugurlar et al, 2018	2.6	0.3	5.2	3.6	20.3%	-2.60 [-3.72, -1.48]	
Jain et al, 2018	3	2.6	3.3	2.8	19.4%	-0.30 [-1.48, 0.88]	
Shettyet al., 2019	3.3	2.9	4.8	2.9	15.7%	-1.50 [-2.97, -0.03]	
Khurana et al, 2020	0.52	0.6	1.92	1.03	32.2%	-1.40 [-1.70, -1.10]	
Total (95% CI)					**100.0%**	**-1.22 [-2.02, -0.42]**	



Heterogeneity: Tau²= 0.49; Chi²= 11.623, df=4 (P=0.02) I²= 66%
Test for overall effect Z=3.00 (P=0.003)

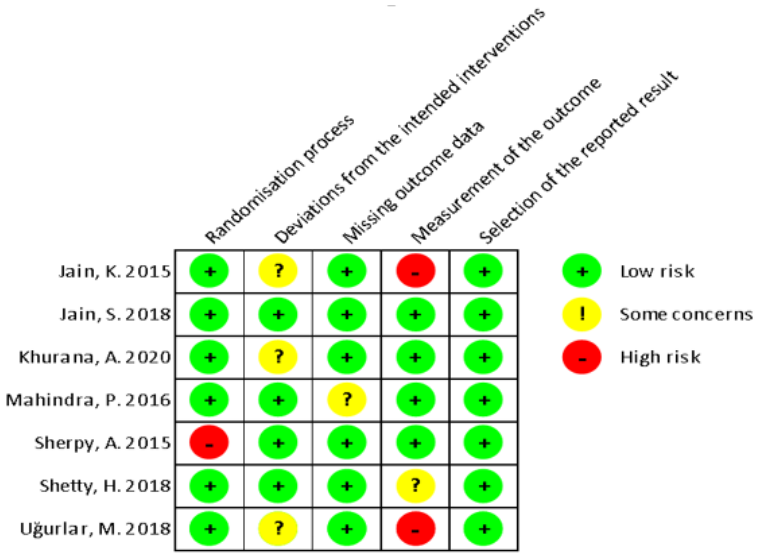


Figure 1: Summary of risk of bias

Pain Appeared 6 Months Post-Injection

We foundfive studies with pain measurement data at 6 months post-injection, as shown in Figure 1 and Table 3. Meta-analysis and Forest Plot showed that PRP injection reduced pain significantly more than corticosteroid injection (WMD: -1.22, 95%

CI:-2.02 to -0.42; p=0.003). Heterogeneity in the study was considered relatively high (Chi^2=11.62; I^2=66%). Of the seven studies that the author uses in a systematic review study, 2 journals examine the thickness of the Fascia plantaris before and after injection, namely the study by Sherpy(2015)[11] and Jain (2018).[7]

A study conducted by Jain revealed that corticosteroid injection can reduce fascia thickness better in the first one month with a mean difference of 0.8 for PRP and 1.4 for Corticosteroids. In the 3rd month, corticosteroid injection (mean difference 1.9) was better than PRP injection (mean difference 1.5). Until the 6th month of corticosteroids (mean difference 2.2) was also still better than PRP injection (mean difference 2.1), although when compared to 3 months, PRP injection was better in reducing thickness. It is stated that corticosteroid injection is better in reducing thickness than PRP injection significantly in the first month and 3rd month after injection. Meanwhile, at the 6th month, there was no significant difference in thickness reduction.

Meanwhile, according to a study conducted by Sherpy, PRP injection can reduce fascia thickness better than corticosteroid injection, both at month 1.5 with a mean difference of 0.5 for PRP and 0.22 for corticosteroids, also at month 3 with a mean difference of 0.99 for PRP and 0.53 for corticosteroids. However, it was stated that the difference between the two injections in reducing thickness was not significant.

All studies reported that there were no complications for neither PRP injection therapy nor corticosteroid injection therapy.

Discussion

Plantar fasciitis is a disease of the feet in pain that greatly interferes with daily activities.[2] Although it is self-limiting or can heal on its own, sometimes plantar fasciitis does not go away even with a combination of conservative therapy, thus requiring continued treatment.[4] Corticosteroid injection is one of the advanced therapies that can be used. Corticosteroid injections have been shown to reduce inflammation and pain in patients with plantar fasciitis quickly and effectively with anti-inflammatory effects that can accelerate the inflammatory process in patients.[7] Even so, complications from corticosteroid injections in the form of fat atrophy and plantar fascia to the occurrence of fascia rupture make researchers look for safer, more effective and efficient alternatives for plantar fasciitis treatment options that do not improve with conservative therapy. Platelet-Rich Plasma or abbreviated PRP is an alternative therapy that can reduce inflammation and pain quickly, and has a low possibility of complications.[8]

This study used the VAS to perform comparisons of pain reduction regardless of the arguments that questioned the subjectivity of the VAS, which resulted in results according to how data takers in each study described pain on the VAS scale. In addition, pain measurement using VAS is also very simple so that it can be done anywhere easily.[11]

The meta-analysis data support the assumption that PRP injection has a better outcome in reducing pain over a longer period of time. In a very short period of 1-month PRP injection and corticosteroids were equally as effective in reducing pain (WMD: 1.22, 95% CI: -1.10 to 3.54; p= 0.30). In the medium term of 3 months, PRP injection reduced pain more than corticosteroid injection (WMD: -0.77, 95% CI: -1.46 to -0.96; p=0.03). Meanwhile, in a long period of 6 months, PRP injection also reduced pain more than corticosteroid injection (WMD: -1.22, 95% CI: -2.02 to -0.42; p=0.003).

Based on the findings, PRP injection and corticosteroids were as much pain relief in the evaluation of the 1st-month post-injection, while at the 3rd and 6th months, PRP injection was more in reducing pain. In the 1st month, RP injection and corticosteroids were equally effective in reducing pain because their function was to inhibit inflammatory genes such as Interleukin and Nuclear Factor kappa B, thereby reducing inflammation, and in the process, inhibiting cyclooxygenase-2, which resulted in reduced pain. In addition to the inhibitory function of inflammatory genes, growth factors in PRP can also increase collagen production, which will help in strengthening fascia and speeding up the healing process. Growth factors can also accelerate cell activities such as cell proliferation, communication, and differentiation which can accelerate the formation of new cells in the healing process.[15] Both processes will work by accelerating the healing process of microtears or small tears that are the main cause of inflammation so that in the longer term, PRP reduces inflammation more optimally. The healing process takes longer, so at the 3rd and 6th-month evaluation after Platelet-Rich Plasma injection, it can reduce pain more than corticosteroid injection.[16]

In addition to comparing pain relief, measurement of thickness in the plantar fascia can also be used to analyze which therapy is better in treating the plantar fascia. Thickening of the plantar fascia is one of the signs that often appears in patients with plantar fasciitis. According to a study conducted by Jain and colleagues, plantar fasciitis sufferers are 100 times more likely to experience abnormal thickening of the plantar fascia (>4.0 mm) compared to normal individuals (Jain et al., 2018). The thickness of the plantar fascia is caused by inflammation of the fascia itself and the response of the body with growth factors that increase fibroblast proliferation and collagen production which causes thickening of the tissue e.[15]

From the two journals that analyzed fascia thickness, the authors concluded that corticosteroid injection reduced thickness more than Platelet Rich Plasma injection in plantar fasciitis patients. This is due to the mechanism of corticosteroids reducing inflammation and swelling and inhibiting fibroblast proliferation and collagen productionfrom reducing fascia thickness more maximally.[17] In contrast to PRP, which although it can reduce inflammation, thereby reducing fascia thickness, PRP also has a growth factor mechanism that increases fibroblast proliferation and collagen production, which actually thickens the fascia, causing the opposite effect and causing PRP to not be able to reduce fascia thickness maximally.[15]

Following one of the researchers' considerations, the use of PRP injections compared to corticosteroid injections is a high possibility of decreasing complications.[8] All studies used reported that there were no complications after PRP injection therapy or corticosteroid injection therapy. Thus it can be concluded that PRP injection is as safe as corticosteroid injection in plantar fasciitis patients.

This study has several limitations. First, there is fairly high heterogeneity, especially in the pain variable; therefore, a random effect model is used. This heterogeneity can be explained by differences in the type of agent used, the method of preparation of the agent (amount, duration and centrifugation system), additional agents, method of administration of the agent, and the volume of agent used. Second, the use of the slightly subjective Visual Analog Scale pain scale as previously described. Third, the number of studies used to use only 7 RCT studies, from 2 databases. In addition, not all studies used to measure pain simultaneously, so in the analysis, all studies in the month that have been determined cannot be used. Fourth, although only RCTs were used to reduce the possibility of bias arising from not randomization in this study, there was one journal that did not sufficiently meet the randomization criteria by Cochrane. In addition, there are 2 journals that do not meet the final outcome measurement criteria according to the criteria determined by Chocrane, for the assessment of bias in RCT studies.

Conclusion

The difference of effectiveness between Platelet-Rich Plasma injection and corticosteroid injection in patients with plantar fasciitis is varied depending on peak period and facial thickness. Corticosteroid injection reduces pain more than Platelet-Rich Plasma injection in the 1st month. In contrast, in a more extended period, namely the 3rd and 6th month, Platelet-Rich Plasma injection is much more effective to reduce pain. Meanwhile, corticosteroid injection can decrease fascial thickness more than Platelet-Rich Plasma injection. Neither Platelet-Rich Plasma injection nor corticosteroid injection effect the complication of plantar fasciitis. Hence, the safety level of Platelet-Rich Plasma injection is as safe as a corticosteroid injection.

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