

# Plantar Fasciitis: Orthobiologics

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## ABSTRACT

Plantar fasciitis (PF) is characterized by plantar medial heel pain, usually present in the morning at the first few steps. Obese individuals, who stand for prolonged periods and who walk on hard surfaces, typically suffer from PF, the most common cause of plantar heel pain in adults. The diagnosis can be achieved through patient clinical history and clinical findings. Stretching exercises, activity modification, and use of several analgesics resolve symptoms in over 80% of patients, while biomechanical factors can be corrected by insoles or various kinds of orthotics or night splints. In the outnumbered group of patients who develop intractable PF, other available strategies are extracorporeal shock wave therapy and corticosteroid injections. Surgical management of PF consists of plantar fascia release, but efficacy is still debated. In recent years, biological treatments have been getting popularity in many orthopedic conditions.

**Keywords:** Biologics treatment, Bone marrow aspirate concentrate, Plantar heel pain.

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## BACKGROUND

Plantar fasciitis (PF) is usually solved with conservative treatment, but some cases are challenging to manage. New biological therapies have been suggested for multiple soft tissue problems and are gradually gaining the interest of scientific world in this condition as well.

## PLATELET-RICH PLASMA

Platelet-rich plasma (PRP) is a device used for several chronic degenerative soft-tissue conditions, including PF. To prepare PRP, patient's own blood is centrifuged to obtain an increased platelet concentration. Platelet alpha-granules contain growth factors and mediators [vascular endothelial growth factor (VEGF), transforming growth factor-beta 1 (TGF- $\beta$ 1), epidermal growth factor (EGF), platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), insulin-like growth factor 1 (IGF-1)], which are concentrated through a single- or double-centrifugation process. Supraphysiological amounts of these cytokines and growth factors are injected to injury site and promote the physiological healing process.<sup>1–10</sup> Platelet-rich plasma is postulated to promote native tissue regeneration.<sup>11</sup>

Platelet-rich plasma injection efficacy in the management of chronic PF has been evaluated in several randomized controlled trials. Platelet-rich plasma is not associated with the complications of corticosteroid injections, such as, plantar fascia rupture or fat pad atrophy.<sup>12</sup>

Platelet-rich plasma injections were compared to corticosteroid injections by two recent meta-analyses, they conclude that PRP injections were a valid alternative to corticosteroid injections with some studies demonstrating superiority of PRP.<sup>13–15</sup>

Ragab and Othman assessed 25 patients managed with a single injection of PRP. The average visual analog scale (VAS) pain decreased from 9.1 to 2.1 after 1 year postintervention.<sup>16</sup>

After 1 year, a marked improvement in terms of VAS after PRP injection (from 7.1  $\pm$  1.1 to 1.9  $\pm$  1.5) was reported in a prospective uncontrolled study by Martinelli et al.<sup>17</sup> (Table 1).

Sami et al. evaluated the use of PRP injections under ultrasonography guidance to physiotherapy. They prospectively

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recruited patients suffering from chronic PF and divided them into two treatment groups (PRP group vs physiotherapy group). All patients were evaluated using the American Orthopaedic Foot and Ankle Society (AOFAS) score before and after treatment. The AOFAS score improved significantly in the PRP group. Ultrasonography was performed before and 4 weeks after treatment, fascial echogenicity was significantly changed in most of the patients after PRP injection, and fascial thickness was statistically decreased in the PRP group compared to the physiotherapy group.<sup>18</sup>

A comprehensive systematic review analyzed the use of PRP in the treatment of PF.<sup>19</sup> Most the studies analyzed mentioned a

**Table 1:** Success rate of platelet-rich plasma injection therapy

References	Success definition	Success rate (%)
Kumar et al. (2013) <sup>20</sup>	Patients' satisfaction at the question "would have the procedure again"	64
Martinelli et al. (2013) <sup>17</sup>	ReM excellent and good	78.6
Ragab and Othman (2012) <sup>16</sup>	Satisfaction at patient's questionnaire	88
Aksahin et al. (2012) <sup>21</sup>	ReM excellent and good	33.3

significantly larger improvement in symptoms between the first visit and the last follow-up evaluation.

Platelet-rich plasma injections are an effective option to decrease pain and enhance function in chronic PF and may be safer and more efficient than corticosteroid injections.<sup>16</sup>

### Corticosteroid vs Platelet-rich Plasma

Different studies analyzed the use of corticosteroids injections vs PRP in patients with PF using functional evaluation and pain scales.

Monto recruited 40 individuals with chronic unilateral PF who had failed traditional conservative treatment. They were randomized into two groups:<sup>14</sup> Group I was managed with only ultrasound-guided injection of 40 mg DepoMedrol (methylprednisolone), and group II with one ultrasound-guided injection of autologous PRP.

Average AOFAS score before treatment was 52 in the cortisone group, improving to 81 at 3 months posttreatment and decreasing to 74 at 6 months, at 12 months it dropped to 58 and persisted to decay to a final score of 56 at 24 months. Conversely, average AOFAS score was 37 in the PRP group before treatment and raised to 95 at 3 months, remaining elevated at 94 at 6 and 12 months, and reaching a final score of 92 at 24 months.

In patients with severe chronic PF who have not obtained the wished result to traditional conservative management, PRP is able to provide successful benefits in the long-term, being more efficacious than corticosteroid injections, and appearing safer than surgical alternatives.<sup>22</sup>

In the controlled, randomized, blinded clinical study by Acosta-Olivo et al.,<sup>23</sup> patients were randomized into two groups. Administration of dexamethasone 8 mg plus 2 mL of lidocaine was adopted in the steroid treatment group, while 3 mL of PRP activated with 0.45 mL of 10% calcium gluconate was used in the PRP treatment group. The VAS, Foot and Ankle Disability Index (FADI), and AOFAS scale were proposed to all patients at the beginning of the study, and at 2, 4, 8, 12, and 16 weeks posttreatment.

Platelet-rich plasma was a valid strategy when patients with PF failed to respond to nonoperative treatment. The PRP efficiency was comparable to that of steroids injections, without complications associated with steroid use. On the contrary, there are some disadvantages: PRP is more costly than steroids; the process to obtain PRP is time expensive for patients and physicians. In addition, PRP reduces inflammation and promotes the regeneration of damaged tissue, especially soft tissues, in particular muscles and tendons, thanks to its regenerative proprieties.

In conclusion, the use of PRP seems more efficacious than corticosteroid injections.

### Prolotherapy

Prolotherapy is an injection-based treatment used in chronic musculoskeletal conditions, such as, PF. In this procedure, a natural irritant (such as, hyperosmolar dextrose) is injected into the soft tissues of the plantar fascia to cause the osmotic rupture of local cells and trigger a healing response. Prolotherapy injections can be effective in patients with chronic PF.<sup>24–26</sup> The efficacy of a prolotherapy injection is superior to that of corticosteroids, as it allows tissue healing similar to PRP.<sup>27</sup> Prolotherapy injections are simpler to prepare than PRP, noninvasive, and more cost-effective.<sup>28</sup> This procedure is considered safe and efficacious, with only minor reported adverse effects mainly pain or discomfort at the site of injections.<sup>29</sup> Uğurlar et al. compared the use of extracorporeal shock

wave therapy (ESWT) to corticosteroids, PRP, and prolotherapy injections for the treatment of PF through a randomized controlled prospective clinical trial. The VAS and Revised Foot Function Index were used to evaluate the clinical outcomes. The corticosteroid injection reduced foot pain in the first 3 months, while ESWT had similar results in the first 6 months. The result of prolotherapy and PRP was seen during the follow-up period, while the corticosteroid injection lost its effectiveness. Nevertheless, at the 36-month follow-up point, no significant difference was noted in terms of VAS and Revised Foot Function Index score among the four treatments.<sup>30</sup>

### Bone Marrow Aspirate Concentrate

One promising new non-surgical treatment is bone marrow concentrate (BMC) or bone marrow aspirate concentrate (BMAC) therapy.<sup>31</sup> Bone marrow aspirate concentrate is obtained by centrifugation of autologous bone marrow aspiration. Bone marrow aspirate concentrate is composed of a concentration of mesenchymal stem cells (MSCs), white blood cells, hematopoietic stem cells (HSCs), growth factors, and platelets.<sup>32</sup> After centrifugation, the percentage of MSCs in BMAC varies from 0.001 to 0.01% of mononuclear cells. However, growth factors, including PDGF, transforming growth factor-beta (TGF- $\beta$ ), bone morphogenetic protein (BMP)-2, and BMP-7 with their anabolic and anti-inflammatory effects, can be found in BMAC.<sup>33</sup>

Recently, there has been much curiosity in the use of BMAC in orthopedic field. Much of the focus on the benefits of BMAC in musculoskeletal ailments is on the potential of MSCs to differentiate into various cells and tissues originated from mesenchymal cells.<sup>34,35</sup> Inflammatory process, mechanical stress, degenerative changes, and disorganized healing are all mechanisms of tendon injury. Bone marrow aspirate concentrate promotes tenocyte proliferation to enhance the recovery and healing of injured tendons.

Many theories have been suggested to understand the cellular healing promoted by BMAC: Cells contained in BMAC modulate the healing process of pathological tendons controlling inflammation, recruiting other cells, such as, tenocytes and MSCs, to ensure regeneration and reduce fibrosis.<sup>36</sup> Courneya et al. showed that IL-4 and IL-13 contained in BMAC stimulate the proliferation of human tenocytes. Vascular endothelial growth factors are also included in BMAC to aid healing.<sup>37</sup>

### CONCLUSION

Conservative treatment is successful in most patients with PF. Physicians need to bear in mind that early diagnosis and management usually lead to a shorter treatment as well as increased chance of success with conservative measures.

Strengthening and stretching programs play a key role in the management of PF, and must be recommended in addition to biological treatments.

The current widespread use of corticosteroids must be discouraged because of the adverse reactions and the limitation of their prolonged use.

Biological treatments are becoming a viable management option because of their low risks for the patient, and their sustainability. In addition, less known types of injections are becoming more fashionable, such as, botulinum toxin-A injections, providing significant pain relief.<sup>38,39</sup>

In some cases, after 6 or more months of conservative treatment, it is necessary to try more invasive options. Surgical

release of the plantar fascia is an available option when biological measures are not effective, but it is destined to a small proportion of patients. New techniques, such as, endoscopic plantar release, may play a role.

Usually, PF is a self-limiting condition, but time until resolution ranges from 6 to 18 months, leading to frustration for patients and physicians.

Patients' regular activities can be compromised by chronic heel pain; physicians can prevent this condition using the right conservative measures.

Further randomized double-blinded controlled trials need to be undertaken, especially to demonstrate whether in most cases heel pain disappears because of treatment or because of its natural course.

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