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# Key Insights On Platelet-Rich Plasma For Soft Tissue Repair

While platelet-rich plasma (PRP) has emerged as a potential regenerative modality to some lower extremity injuries, there is a lack of high-quality literature. This article provides a review of the current literature on PRP for soft tissue repair. The author reviews the use of PRP for the treatment of acute and chronic plantar fasciitis.

By Sean C. ...

**W**hile oral maxillofacial surgeons have been utilizing platelet rich plasma (PRP) for over a decade, PRP has become an increasingly hot topic in the realm of musculoskeletal pathology in recent years.<sup>1</sup>

Technicians would obtain PRP by obtaining a small amount of blood via IV puncture and separating the whole blood components from the platelets typically through the use of a centrifuge. The PRP contains numerous growth factors, including insulin-like growth factors (ILGF) 1 and 2, transforming growth factor- $\beta$  (TGF- $\beta$ ), vascular endothelial growth factor (VEGF), fibroblast growth factor and hepatocyte growth factor, to name a few. The type and amount of growth factor are patient dependent.

The basic science behind PRP is fairly simple. Platelet rich plasma is simply defined as a sample of autologous blood with concentrations of platelets that are typically five times greater than baseline levels. The science of PRP basically involves the alpha-granules found within the platelets. Alpha-granules contain growth factors that affect all aspects

of the healing cascade to facilitate healing of all types of tissue. The growth factors are proteins that are secreted and bind to a receptor on a membrane to exert a response from the cell, which leads to the healing response. Examples of these target cells are osteoblasts, fibroblasts, endothelial cells, epidermal cells and mesenchymal stem cells (MSCs). There is a high amount of interest in the use of PRP for soft tissue injuries but high quality literature is lacking.

There are several companies that have the capability of producing the PRP. The concentration typically consists of a separation of red blood cells, platelet concentration and platelet-poor plasma. The amount of blood that is needed to produce the PRP differs among the companies. Activation may occur with or without adding an activating agent. One may add thrombin and/or calcium chloride to begin platelet activation, formation of the clot and release of the growth factors. Some studies have shown the use of thrombin can inhibit bone formation with the use of demineralized bone matrix.<sup>2</sup>

The other option is not to use the acti-

vating agent. Reports by Mishra, Fufa and their respective colleagues have shown that the exposure of PRP to tendon derived collagen factor alone can cause a slow and sustained activation.<sup>3</sup>

Tendon and ligament injuries are both subdivided into acute and chronic injuries. Acute injuries involve tearing of collagen fibers; hematoma formation and subsequent healing through inflammation, cellular proliferation, regeneration and repair, and remodeling processes.<sup>4</sup> On the other hand, chronic injuries are often associated with overuse and lead to a degenerative process. Tendinopathy involves collagen fiber disruption, matrix regeneration, neovascularization and the absence of inflammation.<sup>5</sup>

## What The Literature Reveals About Treating Acute Injuries With PRP

Animal studies by Barreau and co-workers have shown that specific growth factors such as TGF- $\beta$  improve healing and mechanical strength in early ligament healing. The greatest response occur-

ring within the first 24 hours.<sup>7</sup> In another animal study, Murray and colleagues found the application of PRP facilitated early improvement in load to failure, maximum load and stiffness of porcine anterior cruciate ligament (ACL) suture repairs. However, they noted no improvement in laxity, maximum tensile load or linear stiffness with longer follow-up.<sup>8</sup>

While basic science does show early enhanced healing in acute injuries with PRP application, randomized controlled studies involving humans have failed to show an improvement over conventional methods.

In my experience, I have used PRP to treat acute tibiofibular ligament high ankle sprains in college level athletes and performed the injection within 48 hours after the injury. These athletes were able to return to competition seven to 10 days after the injury using a protective ankle support.

Animal studies by Kajikawa and colleagues show that macrophages and fibroblasts are present in the early stages in tendon healing but decrease over time.<sup>9</sup> Platelet-rich plasma enhanced the number of fibroblasts in tendon and the amount of collagen synthesis in the initial stage after tendon injury, according to another study by Kajikawa and co-workers.<sup>10</sup>

Research has shown that single PRP injections increase tendon strength to failure, stiffness and ultimately the amount of stress that the tendon can withstand in the early stages of healing.<sup>11-13</sup>

Aspenberg and Virchenko transected the Achilles tendon in rats and removed a 3 mm segment of tendon.<sup>11</sup> The percutaneous injection of a platelet concentrate into the hematoma increased tendon callus strength and stiffness by about 30 percent after one week, an effect the authors say persisted for as long as three weeks after the injection.

In a study of 48 rabbits, Lyras and colleagues noted the presence of significantly more angiogenesis in those injected with PRP in comparison to the control group during the first two weeks of the healing



Here one can see placement of the platelet-rich fibrin clot in an Achilles tendon tear. The author's preferred method of PRP is the use of a platelet-rich fibrin clot in order to suture the clot directly into the substance of the tendon.



This photo shows the repaired Achilles tendon. The author has treated 25 patients with Achilles tendinosis with PRP injections, all of whom previously failed conservative treatment including immobilization and physical therapy.

process.<sup>12</sup> In another study of rabbits, Lyras and colleagues showed that PRP may affect the tendon healing process by altering the expression of TGF- $\beta$  1.<sup>13</sup>

Sanchez and colleagues performed a case-control study looking at the use of a preparation rich in growth factors (PRGF) in the repair of acute Achilles tendon ruptures.<sup>14</sup> Six athletes who had a complete Achilles tendon tear had open suture repair and also received PRGF injections in comparison to six athletes who received surgical treatment without PRGF. The adjunctive PRGF group demonstrated an earlier return to range of motion, an earlier return to gentle running and earlier re-

sumption of sports training activities. The study's main disadvantage is a low number of patients.

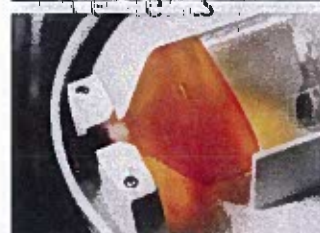
In contrast to this study, another randomized controlled trial by Schepull and colleagues compared 30 patients who had repair of an acute Achilles rupture.<sup>15</sup> Sixteen patients received an injection with PRP prior to skin closure and 14 patients received no injection. The Achilles Tendon Total Rupture Score showed no significant difference at one-year follow-up in the heel raise index between the groups. In fact, the Achilles Tendon Total Rupture Score was significantly lower in the PRP group.

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This photo shows the treatment of the plantar fascia with PRP under ultrasound guidance. The author has used PRP to treat chronic plantar fascial pain, noting that his patients with chronic plantar fascial pain previously failed conservative treatment with orthotics, steroid injections, nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy.

There is a lack of high quality studies that prove or disprove the use of PRP in the treatment of acute tendon injuries.

I have used PRP with repair of acute Achilles tendon ruptures or tears successfully over the last three years. The preferred method is the use of a platelet-rich fibrin clot in order to suture the clot directly into the substance of the tendon.

## Exploring The Potential Of PRP For Chronic Tendinopathy

Chronic tendinopathy typically has a histological appearance of collagen fiber disruption, mucoid degeneration, neovascularization and a lack of inflammation.<sup>6</sup> Researchers have suggested the use of PRP for chronic tendinopathy improves angiogenesis and collagen synthesis.<sup>16,17</sup>

Achilles tendinosis or chronic tendinopathy is one of the most studied tendon injuries in regard to the use of PRP. A randomized control trial by de Vos and colleagues evaluated the effec-

tiveness of injecting 4 mL of PRP into degenerated areas in the Achilles tendon using Doppler ultrasound guidance in comparison to a placebo saline injection.<sup>18</sup> The authors found that both groups had similar improvement based on the Victorian Institute of Sports Assessment-Achilles (VISA-A) score and a similar rate of return to sports. However, the authors elected to inject both groups prior to the start of physical therapy.

Conservative treatment with physical therapy, especially eccentric exercises, is known to treat chronic Achilles tendinopathy effectively.<sup>19</sup> So one might argue that the effect of PRP or the placebo would have been masked because most patients will likely respond favorably with the use of eccentric therapy.

Gaweda and co-workers evaluated the effectiveness of PRP on non-insertional Achilles tendinopathy.<sup>20</sup> Fourteen patients (total of 15 tendons) had a 3 mL

PRP injection under the ultrasound guidance into the degenerated portion of the Achilles tendon. The authors emphasized protected weight bearing for six weeks. Six patients required a repeat injection.

Patients were allowed to resume normal daily activities between two weeks after the injection. Patients who began nor sporting activities were discouraged at this time. Researchers evaluated patients with the American Orthopaedic Foot and Ankle Society (AOFAS) score and the VISA-A score. Both the AOFAS and the VISA-A scoring proved significantly from baseline. Both the AOFAS and the VISA-A scores improved from 55 to 96 at 18 months. The authors also noted a decrease in fusiform thickening, respectively, thickening, hypoechoic foci and intratendinous tears.

## A Closer Look At The Author's Experience With PRP

I have treated 25 patients with Achilles tendinosis with PRP injections. All patients failed conservative treatment with immobilization and physical therapy. The PRP injection was attempted to avoid formal surgical debridement of the Achilles tendon.

The patients received a 5 to 7-mL PRP injection in addition to a gastrocnemius recession. I performed the procedure under a general anesthetic. I performed the procedure with patient in the prone position. I injected both the Achilles tendon and the paratenon.

The postoperative protocol involved two weeks of weight bearing in a protective cast boot as tolerated. Patients wore the boot for 24 hours during the first two weeks. At the two-week follow-up, the patients were allowed to wear shoes as tolerated and to resume normal activities.

sleep in a night splint for the next four weeks. At six weeks post-op, I re-evaluated the patients.

The patients subjectively rated their improvement as 75 percent (16 of 25 patients), 50 percent (six patients) or 25 percent improvement (three patients). Patients who noted 75 percent improvement were allowed to advance activities as tolerated. For patients who noted 50 percent improvement, I performed another PRP injection. For those who had 25 percent improvement, I considered PRP unsuccessful and gave these patients the option of open Achilles debridement.

Sixteen of the 25 patients had 75 percent improvement or better, and returned to normal activities. Three patients had less than 25 percent improvement with PRP and all three went on to formal debridement. The remaining six patients had 50 percent improvement.

All patients with 50 percent improvement received a second PRP injection six to nine weeks after the initial surgery. I performed the second injection as an outpatient procedure with the patients under sedation. The patients wore a walking boot for seven days and were allowed to advance into shoes at that point.

Four of the six patients improved and have not required further surgery. One of the remaining two felt that the improvement was enough to continue with normal activities and has not proceeded with other treatment. The other patient had open debridement.

Obviously, the major limitation with this study is that all patients had a gastrocnemius recession, which alone could have led to the improvement. The longest follow-up is three years.

I have also used PRP to treat chronic plantar fascial pain. While the patients' usual presentation is typical of plantar

fasciitis, they no longer have signs of inflammation consistent with plantar fasciitis. These patients, with chronic plantar fascial pain, with chronic treatment with oral conservative medications, nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy.

Surgical intervention consists of a gastrocnemius recession with PRP injection into the medial arch of the foot. The plantar fascia originates from the medial malleolus of the talus and is the same as the posterior tibial tendon. I have followed 51 patients for three years. Preliminary results are as follows:

51 patients had 90 percent success with PRP injection. Five patients received an open plantar fasciectomy again, the major limitation of this study. One result is that patients with gastrocnemius recession.

## In Conclusion

The biochemistry of PRP for the treatment of musculoskeletal issues seems to be effective. Although there is a lack of well designed, high-level evidence, the clinical significance of PRP

for the treatment of musculoskeletal injuries of ligaments and tendons may employ PRP as a less invasive surgical procedure.

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