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Platelet-Rich Plasma?

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ABSTRACT

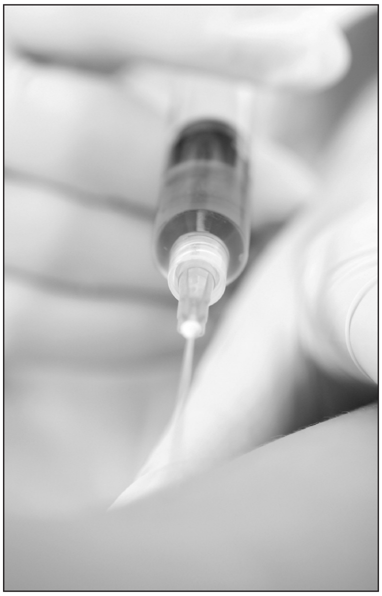
Platelet-rich plasma (PRP) is rapidly becoming a prominent method of treatment among sports medicine professionals. Yet research examining the efficacy of PRP has yielded mixed results. The type of PRP, along with the appropriate timing and number of injections, must be considered to assess treatment outcomes. In addition, post-PRP protocol must be implemented properly to yield positive results.

Muscle, ligament, and tendon injury account for a significant loss of playing time among athletes. Moreover, these injuries account for more than 100 million office visits per year.[1] As sports medicine professionals, our top priority is to find and develop methods that allow our athletes to heal quickly and return to the playing field in record time. Recently, there has been a significant increase in the use of platelet-rich plasma (PRP) to help accomplish this goal. But is PRP the magic bullet we have been waiting for? The answer, simply, is we do not know yet. The conflicting evidence that surrounds the use of PRP treatment stems from a variety of reasons; as such, we will discuss a few of the variables that seem to play a major role in determining the outcome of PRP treatments in athletes and the general outpatient population.

Over the past 2 years, sports medicine physicians at the University of North Carolina at Chapel Hill have been using PRP with some good results; however, the published data are inconclusive at best.

Two recent journal articles have demonstrated mixed results. Peerbooms et al[2] randomized 100 patients with lateral epicondylitis experiencing pain for more than 6 months into 2 groups. Patients in the first group (n = 51) were treated with autologous PRP injection, and those in the second group (n = 49) were treated with a corticosteroid injection. A similar injection technique for both procedures was delivered directly into the patient's most painful area.

Successful treatment was defined as a 25% reduction in pain using the Disability of the Arm, Shoulder, and Hand (DASH) Outcome Measure score and the visual analog score (VAS). After a 1-year follow-up period, Peerbooms et al[2] found that patients in the PRP treatment group experienced greater treatment success in VAS and DASH scores compared with the corticosteroid group. These differences were found to be statistically significant ($P < .001$ and $P = .005$, respectively). Of note, the steroid injection group showed a more favorable response 4 weeks after treatment. However, the PRP group continued to improve throughout the year, whereas the steroid group showed a regression.[2]



In a second study, de Vos et al[3] examined the use of PRP in Achilles tendinopathy. This double-blinded study randomized patients experiencing pain for more than 2 months into 2 groups. Participants in one group (n = 27) received a single injection with autologous PRP, and

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those in the other group (n = 27) received a normal saline injection. The Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire was used to assess the primary outcomes of pain and activity. After a 3-month follow-up period, de Vos et al[3] found that these groups did not have statistically different increases in VISA-A scores (21.7 and 20.5, respectively) across either of the 2 treatment groups. In addition, there were no statistically significant differences between the secondary outcomes: subjective patient satisfaction, return to sports, and adherence to eccentric exercises.[3]

The next logical question is why is there so much variation in PRP treatment outcomes? Platelet-rich plasma is a concentrate that contains approximately 3 to 5 times more platelets than the normal concentration of platelets in human blood. Platelets are small cells that are derived from megakaryocytes formed in bone marrow; they promote blood clotting and wound healing. Platelets are the smallest of all of the blood cells, yet are rich in several growth factors and cytokines that are contained in alpha granules inside the platelets. In effect, these cells are integral to the healing process. Furthermore, PRP helps promote the 3 stages of healing—inflammation, proliferation, and remodeling.[4] Thus, we often reach the conclusion that anything that helps promote healing must be good for our athletes and patients. However, this is not necessarily correct and is precisely where the intricacies of PRP become extremely complicated.

Although PRP has been shown to be safe and efficacious in muscle, tendon, and bone healing, it is important to highlight that there are different types of PRP. These differences include the number of cells, the type of cells,

TABLE

University of North Carolina Sports Medicine Patellar Tendinosis Platelet-Rich Plasma (PRP)

REHABILITATION PROTOCOL
Phase I: Week 1
The goal of this phase is to allow the deep fibers of the patellar tendon to start to heal. The patellar tendinosis occurs in the deep fibers. The tendonotomy was performed in this area and the PRP was injected into this area. Because of this, the fibers will be weak. Days 1-3, the athlete will be on crutches. Days 4-7, the athlete can come off of the crutches and resume weight bearing. No running or explosive activities can be performed during this period. The athlete can ice as needed for pain and any swelling. The athlete should not use any nonsteroidal anti-inflammatory drugs for at least 14 days because this can prevent the PRP from working well. The athlete can take acetaminophen and will be given a prescription for oxycodone with acetaminophen after the procedure.
Phase II: Week 2
Begin range-of-motion (ROM) exercise:
Gastrocnemius/soleus, hamstring stretches
Single-leg raises in 4 planes in full extension
Resisted ankle ROM with Thera-band (The Hygenic Corporation, Akron, Ohio)
Heel slides from 0° to 90°
Continue cryotherapy for any swelling and pain
Phase III: Week 3 and 4 as long as pain free (soreness is OK)
Continue with ROM/flexibility exercises
Quadriceps, hamstring, iliotbial band, gastrocnemius/soleus flexibility
Work on normal gait with some stair climbing as long as it is pain free
Increase strength in the hip (4-way hip), quadriceps, hamstring, and calf muscles
Ok to include leg press, one-leg squats, step up, partial lunges, deeper wall sits (start short with all of these and then progress deeper as pain allows)
Core strengthening
Proprioceptive/balance activities: ball toss, balance beam, emphasize hip and knee flexion
Conditioning
Pool running, stationary bike, elliptical machine
Phase IV: Week 5 as long as the patient tolerated the previous phase and has no pain in knee
Continue with ROM/flexibility and strengthening exercises
Progress strengthening
Progress to eccentrics (isolated quadriceps)
Progress to running and continue other conditioning exercises
Side steps
Crossovers
Figure 8 running
Shuttle running
One-leg and two-leg jumping
Cutting
Agility ladder drills
Initiate sport-specific drills and plyometric program
Phase V: Week 6
Full return to play

and the concentration of growth factors found in the concentrate. All of these factors are determined by the system used to make PRP. Thus, although some companies believe that the higher the number of cells and growth factors, the better, this is not true.

For example, many studies have shown that the growth factor TGF-beta, found in PRP, promotes fibrosis at too high a concentration. This would certainly not lead to improved functioning of an athlete's injured muscle or tendon. In fact, fibrosis has actually been shown to increase rates of reinjury.[4] Then consider that in addition to different systems being used, concentrates will fluctuate depending on the concentration of cells in the patient's own blood.

The next factor that must be considered is the timing and number of injections. There are many factors that influence the 3 phases of healing. Cytokines, growth factors, and bioactive factors are all active at different phases of this process. For this reason, it is difficult to determine the appropriate time to use PRP. It has been recommended that PRP not be used in the first 24 hours after injury.[5] Other than this recommendation, there are currently no formalized recommendations regarding the number of injections or the timing of those injections. For example, some physicians may give up to 3 injections 2 weeks apart. This can be very expensive because the cost of PRP treatments can range from $500 to $2000.

Obviously, further studies are needed to determine the appropriate PRP timing, number of treatments, and information on the kinetics of cytokine release from different preparations of PRP. Our experience has shown that the majority of injuries, with the exception of athletic pubalgia, will respond to 1 injection. Our protocol for treatment of this disorder requires 2 injections given 1 week apart. Our results have shown that this disorder responds better to multiple injections.

The final, and probably most critical, step is the post-PRP protocol. Protocol implementation ensures that protective measures are in place for the treated area, which is important because PRP has some nociceptive properties. These properties allow the athlete to experience diminished pain before the healing process has been completed. As a result, the athlete is at risk for reinjury. In addition, post-PRP protocols will lead to increased compliance with therapy and provide the athlete, patient, or physical therapist with the information needed for appropriate rehabilitation.

Although each protocol will vary, all posttreatment protocols must begin with protection of the area treated for approximately 48 hours. This typically means use of a boot, sling, or crutches, depending on the injured extremity. Following the 48-hour protection period, the rehabilitation phase should begin with gentle range-of-motion activities and progression to strengthening of the opposing muscle groups, at which point the muscle tendon unit that was treated can be strengthened and the athlete or patient can be progressed back to full activity as they improve.

Addressing imbalances in flexibility and strength of opposing muscle groups is important to the overall rehabilitation process, such that if these factors are not properly addressed, pain from the injury will eventually return. We believe this may be the primary reason that the athletic population, with its easy access to supervised rehabilitation, seems to respond to PRP more readily than the general population. We have witnessed an 85% to 90% success rate with our college athletes versus a 65% success rate with our community patients. (See the Table for an example of our patellar tendon post-PRP protocol.) Some sports medicine professionals also advocate the use of prehabilitation to address potential imbalances and strength deficits that may have been responsible for the injury prior to any PRP treatments, especially in the nonathletic population.

Although PRP is a viable option for treatment of athletic injury, there is a lack of clarity regarding the appropriate concentrates, timing, and injury-specific preinjection and postinjection protocols. Inconsistency in these factors could account for the variability seen thus far in research results and clinical experience. Further research of PRP methods and efficacy is needed before it can be hailed as a magic bullet. In the meantime, it is our duty as sports medicine professionals to carefully weigh the pros and cons in each case when determining whether PRP could be helpful in getting our patients back into the game. ■

REFERENCES

1. Mishra A, Woodall J Jr, Vieira A. Treatment of tendon and muscle using platelet-rich plasma. *Clin Sports Med*. 2009;28:113-125.
2. Peerbooms JC, Sluimer J, Bruijn DJ, Gosens T. Positive effect of an autologous platelet concentrate in lateral epicondylitis in a double blind randomized control trial: Platelet-rich plasma versus corticosteroid injection with a 1-year follow-up. *Am J Sports Med*. 2010;38:255-262.
3. de Vos RJ, Weir A, van Schie HT, et al. Platelet-rich plasma injection for chronic Achilles tendinopathy: A randomized control trial. *JAMA*. 2010;303:144-149.
4. Foster TE, Puskas BL, Mendelbaum MR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: From basic science to clinical applications. *Am J Sports Med*. 2009;37:2259-2272.
5. Harmon KG. Muscle injuries and PRP: What does the science say? *Br J Sports Med*. 2010;44:616-617.