AAOS Now

Platelet-rich plasma: What's behind the hype?

By Kay Daugherty and Mary Ann Porucznik

Does science support PRP use in acute soft-tissue injuries?

Although platelet-rich plasma (PRP) has been used for many years in other medical specialties, it has only recently become popular in orthopaedic applications. Media reports of dramatic "cures" in high-profile athletes have helped fuel interest in PRP, resulting in a voluminous collection of publications. A recent literature search identified nearly 5,000 articles on PRP, more than a quarter of which were published within the last 5 years.

Steven P. Arnoczky, DVM, and Regis O'Keefe, MD

The use of the body's own platelets to enhance healing is a seemingly simple concept that raises very complex questions. The PRP Forum, sponsored by *AAOS Now* and held on Feb. 14, 2011, in San Diego, attempted to answer some of these questions by bringing together approximately 50 of the most knowledgeable and experienced clinicians and researchers in the field of PRP therapy. This is the second in a series of articles reviewing the material presented and summarizing the results.

What is it?

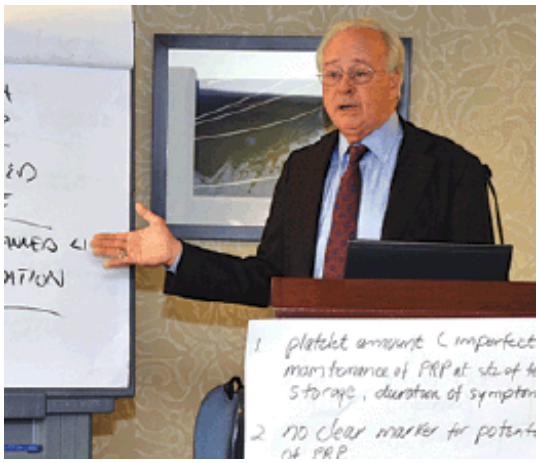
PRP is most simply defined as "a volume of plasma that has a platelet count above the baseline of whole blood." Current PRP preparations, however, can vary markedly in the following ways:

- the amount of blood used and the efficacy of platelet recovery
- the presence or absence of white or red blood cells
- platelet activation with thrombin
- the level of fibrin production

According to **Steven P. Arnoczky, DVM,** "Unlike pharmaceuticals regulated by the United States Pharmacopeia, in which the precise contents, concentrations, and potency are clearly known, PRP preparations have no such guarantee."

Some variations in PRP products may result from differing methods of preparation, but even when specific protocols are used, the platelet concentration of the final PRP can vary greatly among techniques and even within a single technique. In addition, platelet concentrations can vary from day to day in PRP produced from a single individual, depending on factors such as diet, general health, medications (eg, coagulants), and exercise.

"The final platelet (growth factor) concentration will be dependent upon the amount of whole blood used, the platelet recovery efficacy, and the final volume of plasma in which the platelets are suspended," he explained.



James R. Andrews, MD

The two basic steps in preparing PRP include an initial "soft" spin in a centrifugal separator to divide out plasma and platelets from red and white cells, followed by a "hard" spin that further concentrates the platelets into platelet-rich plasma (PRP) and platelet-poor plasma (PPP) components.

The inclusion or exclusion of white blood cells and the presence or absence of a thrombin activator can also cause variations among PRP products.

White blood cells play a key role in the initial phases of inflammation, but have also been reported to increase both muscle damage and the potential for localized pain. "Platelets in microenvironment with white blood cells induce immediate and/or delayed immune response," noted **Allan K. Mishra, MD.**

Combining the PRP isolate with calcium chloride and/or thrombin immediately before injection initiates platelet activation, clot formation, and growth factor release at the injection site. Because growth factors have a very short half-life (minutes to hours), however, thrombin activation could actually decrease the availability of growth factors and diminish the efficacy of PRP to induce bone formation when compared to a non-thrombin activated preparation.

Dr. Mishra also presented a concise classification system for PRP formulations (Table 1) to help compare data from various studies. The system takes into account the inclusion of white blood cells, the addition of a thrombin activator, and the final concentration of platelets.

He noted that PRP is "autologous engineering" a way to help maximize how the body helps heal itself. Stem cells and bone marrow are other examples.

"Patients are seeing elite athletes, like Tiger Woods and Raphael Nadal, being treated with some form of PRP and are asking their orthopaedic surgeons to give them 'what Tiger got.' The problem is that we don't know 'what Tiger got,' what happened to him before or afterwards, or what was used, and no one is publishing that data," noted Dr. Mishra.

"But all three major sports organizations—the National Football League (NFL), Major League Baseball, and the National Basketball Association—as well as the World Anti-Doping Agency, have declared that PRP is a reasonable treatment, despite the fact that we may all agree that there's limited research to support the efficacy of its use," he continued.

Approximately 50 researchers and clinicians attended the half-day forum prior to the 2011 AAOS Annual Meeting.

PRP in soft-tissue injuries

According to Scott A. Rodeo, MD, who discussed the use of PRP in treating acute soft-tissue injuries, most of the data are on PRP for chronic tendinopathy, not for the treatment of acute injury. He reviewed several studies dealing with acute Achilles tendon repair, rotator cuff repair, acute ligament injury, muscle injury, and meniscal repair.

Two studies on the Achilles tendon, for example, found contradictory results. A case-control study concluded that "the operative management of tendons combined with the application of autologous platelet-rich growth factors may present new possibilities for enhanced healing and functional recovery." On the other hand, a small randomized, controlled trial (RCT) found no difference and suggested that "PRP is not useful for treatment of Achilles tendon rupture." But Dr. Rodeo pointed out that both studies were flawed and that the RCT had a strict postoperative casting requirement, which may have affected the efficacy of the PRP.

Three different RCTs have been conducted on using a platelet-rich fibrin matrix (PRFM) for rotator cuff repair, including one conducted by Dr. Rodeo. Although one found support for using PRFM based on patient-reported outcomes such as pain and activities of daily living, the others found no differences in healing or strength.

Despite the fact that no level 1, 2, or 3 evidence exists for use of PRP in muscle injury, noted Dr. Rodeo, a few laboratory studies demonstrate a positive potential for its use, and PRP has been used in the NFL for muscle injuries. Similarly, no data are available on the use of PRP in mensical repair.

"We cannot necessarily extrapolate from studies of chronic tendinopathy, due to the differences in the biologic milieu," noted Dr. Rodeo, "so the timing of the injection is a critical variable in studies of acute injuries."

In discussing the use of PRP for anterior cruciate ligament (ACL) injuries, **Freddie H. Fu, MD,** noted that patients often want to return to sports early. "But the body can heal only so fast," he said, and an early return could predispose them to an increased risk of graft rupture.

Dr. Fu also noted that growth factors, although abundant in the body, may not always be beneficial. Transforming growth factor-beta (TGF-ß), for example, has been shown to cause muscle fibrosis after injury. "Not all growth factors are useful," he said. "We are jumping the gun; it's like giving oxygen to everyone when they don't need it.

"The use of PRP needs to be scientifically driven and not market-driven," said Dr. Fu.

The next article in this series will examine the use of PRP in the treatment of chronic tendinopathy, bone healing, and cartilage defects.

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About the PRP Forum
Cochaired by *AAOS Now* Editor-in-Chief **S. Terry Canale, MD,** and *AAOS Now* editorial board member **Frank B. Kelly, MD,** the PRP Forum, held on Feb. 14, 2011, in San Diego, featured a series of presentations, followed by break-out group discussions, resulting in a series of recommendations for future study of PRP.

Presenters included **Steven P. Arnoczky, DVM; Freddie H. Fu, MD; Wellington Hsu, MD; Elizaveta Kon, MD; Allan K. Mishra, MD; Nicola Maffulli, MD, PhD;** Pietro Randelli, MD; and **Scott A. Rodeo, MD.** Support for the PRP Forum was provided by unrestricted educational grants from Arteriocyte Medical Systems and Zimmer, Inc.

Additional Links:

PRP an unproven option, agree forum experts

Update: PRP in orthopaedics

Platelet-rich plasma: Clarifying the issues

Treating tendinopathy with PRP

Practical guidelines for using PRP in the orthopaedic office

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