**The 1, 2, 3's of Platelet Rich Plasma: Know What's in Your PRP**

Owing in part to famous athletes like Tiger Woods, Peyton Manning, and Alex Rodriguez touting its benefits, the use of platelet rich plasma (PRP) has grown in popularity over the last decade. The healing capacity of PRP has expanded into many applications as evidenced by more than 1,100 clinical trials registered on ClinicalTrials.gov. Still, there remains some questions regarding which applications are most appropriate for PRP, what is the ideal dose (1, 2 or 3 applications) and which PRP system (s) have demonstrated favorable outcomes in peer-reviewed literature.

Recognized as a potent adhesive and hemostatic agent since the 1970s and a robust source of autologous growth factors since the 1990s, PRP is a form of regenerative medicine centered on the science that platelets are instrumental in the body's natural healing process. A PRP procedure involves drawing a small amount of the patient's blood, spinning it in a centrifuge to separate the red and white blood cells from the platelets and then strategically delivering the concentrated platelets in plasma (the liquid part of blood) into damaged tissue to stimulate the healing cascade. In most PRP treatments, the process takes less than thirty minutes to prepare and administer.

Take SELPHYL®, for instance, a popular PRP system from Factor Medical and branded as "The Next Generation of PRP" because, amongst other reasons, its fibrin polymerization is hypothesized to provide a protracted platelet delivery compared to traditional PRP. Nine to eighteen 9-18 ccs of a patient's blood are drawn into blood collection tubes where a proprietary gel separates red blood cells (RBCs) and leukocytes from the platelets using a 6-minute centrifugation process. It is common school of thought in the industry that removing RBCs and particularly leukocytes, can be beneficial to the healing process because leukocytes release cytokines which can exacerbate the inflammatory response to damaged tissue (e.g., leukocyte-poor PRP).

**Three Simple Questions to Differentiation PRP Systems**

Amongst other things, physicians need to be aware of the leukocyte variable and biologic activity in determining their ideal PRP system. There are dozens of different options on the market and, safe to say, not all PRP systems are created equal (not even close). To differentiate, medical providers offering PRP to their patients can start by asking three simple questions:

1. Does the PRP system have peer-reviewed basic science and clinical data?
2. Does the PRP system produce leukocyte-poor or leukocyte-rich PRP with red blood cell contamination?

3. Does the PRP system have good economics for the physician and patient, especially in a self-pay scenario?

These three questions provide a treasure trove of vital information to PRP decision makers. As it happens, most PRP manufacturers won't be able to answer "yes" to all three in direct response to the product they're providing. Some common responses are that no manufacturer of a PRP system can definitively answer "yes" to these questions because there has historically been a dearth of research that underscore the first two.

The manufacturer of the SELPHYL® leukocyte-poor PRP system embraces comparisons and encourages physicians to read any number of the peer-reviewed data and publications that support the use of their PRP. Once a fraction of the data is consumed, the differences begin to become more evident.

**Leukocyte-Poor or Leukocyte-Rich?**

Being "rich" may not be a good thing in certain circumstances. For example, research performed at Cornell University and published in The Journal of Bone and Joint Surgery in 2012 and on PubMed detailed the investigation of the optimum composition of PRP for the treatment of tendinopathies. Citing white blood cells (leukocytes) contribute to inflammatory cytokine production, the researchers concluded that "leukocyte-reduced PRP may be the optimum preparation to stimulate superior healing without scar tissue formation."

Animal research completed at Stanford University evaluating leukocytes' role in PRP therapy for tendinopathy arrived at similar conclusions. Published in The American Journal of Sports Medicine, the scientists observed a notable early inflammatory response in an animal model, concluding that leukocyte-rich PRP (LR-PRP) derived from the GPS III system (Biomet) "causes a significantly greater acute inflammatory response at 5 days after injection" compared to leukocyte-poor PRP (LP-PRP) collected via the Cascade system from the Musculoskeletal Transplant Foundation (MTF).

Looking to put to rest the LR-PRP vs. LP-PRP question with respect to inflammation, a recent systematic review and meta-analysis evaluated 32 independent studies which showed higher incidence rates for adverse reactions and a significantly higher rate of swelling and pain when PRP systems contained high leukocyte counts compared to PRP systems with reduced leukocytes counts in the same application.

**Mono a Mono (a Mono)**

That's not the only time that leukocyte-rich and leukocyte-poor PRP systems have been compared head-to-head. Separate research at Stanford put Biomet's GPS III, MTF's Cascade, and Arteriocyte's Magellan system through the rigors to better understand concentrations of associated growth factors and white blood cells containing leukocytes.

Some differences were obvious. The Cascade system produced a higher volume of PRP from less blood using a substantially shorter centrifugation spin time (6 minutes vs. 15 minutes (GPS III) and 17 minutes (Magellan)). The research also noted a difference in platelet capture efficiency, with Cascade again coming out on top. Probably the most striking difference was the significant variability of the resulting PRP produced from GPS III (standard deviation of 51.7%) and Magellan (standard deviation of 31.6%) compared to Cascade (standard deviation of 5.6%) suggesting that the Cascade system delivers the most consistent and reproducible PRP of all systems compared in the study. These data are very important when counselling patients on which applications may be appropriate for PRP and what to expect from the PRP system used for their treatment.

**Good Economics, Peer-Reviewed Data and Consistent PRP Systems**

From high profile athletes to weekend warriors, PRP has been widely adopted by physicians and patients as a viable solution for a variety of orthopedic and other applications. Harnessing a patient's own platelets and associated growth factors is an attractive and natural approach to potentially augment the healing cascade in connective tissue. Indeed, there has been some disconnected research results, which may be attributed to standardization in methods and the fact that LR-PRP and LP-PRP are similar but not the same. The question of whether a PRP system, without leukocytes, may be more beneficial for certain applications appears to have some merit. It is also quite clear that not all PRP systems are created equal; volume of blood required to produce PRP, the amount of time it takes, the consistency of the final product and cost are all key factors in the decision process. Asking a few basic questions about the published data, the presence or absence of leukocytes and overcall economics will provide the needed insight to better educate patients on the benefits of a specific PRP system and which applications may be appropriate for a PRP treatment.