Platelet-rich Plasma: Is It the Future of Ligament and Tendon Injury Care?

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The use of regenerative medicine has become increasingly popular in both human and veterinary medicine for a variety of disease processes. The goal of regenerative therapies is to stimulate damaged tissues to heal, or regenerate, to their normal functioning state. Stem-cells are the most common form of regenerative medicine studied and used in clinical practice. However, other types of regenerative medicine, such as tissue engineering and utilizing biologically active molecules to stimulate regeneration, are also being used and studied. Platelet rich plasma (PRP) is a regenerative medicine therapy that is thought to hasten healing of tissues when applied directly to the site of injury. PRP was first used in 1987 by Ferrari et al. to seal an incision during open heart surgery in hopes of reducing the need for an excessive transfusion volume. Since its original debut, a plethora of case studies have been published within the human literature documenting the safe use of PRP in oral surgery, periodontal surgery, neurosurgery, ophthalmology, wound healing, bone healing, joint replacements, and more recently, sports medicine injuries. The use of PRP for athletic injuries is an area of intense research and clinical applications. However, its clinical use has outpaced scientific studies and large scale clinical trials qualifying the advantageous use of PRP.

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What is Platelet-rich Plasma and How Does It Work?

Platelets are the smallest cell type found in blood and are largely known for their role in hemostasis (clotting of blood) and wound healing. Platelets circulate in the body in an inactive state and have an average life span of 7-10 days. They require a stimulus, like injury to a blood vessel, to trigger them into action. Once activated, platelets become sticky, which allows them to adhere to a damaged region of a blood vessel and to one another. This results in the formation of a “patch” or clot over the traumatized area of the blood vessel. Platelets also contain two types of granules: one that contains serotonin, thromboxane, histamine, dopamine, calcium, and adenosine, and one that carries bioactive growth factors. The first granule type increases vascular permeability, which allows access of inflammatory cells to the site of damage and contributes to the clot formation.

The second type of granule releases the growth factors, stimulating other cells in the body to migrate to the area of trauma, thus facilitating tissue healing. Various growth factors identified within the platelets have been named, and all have acronyms by which they are referred to. The two factors that are thought to have the most influential role in wound healing are transforming growth factor-beta (TGF-β) and platelet-derived growth factor (PDGF). It is the growth factors contained within the platelets that are of significance for use in tissue injuries.

In dogs, the normal platelet concentration is 200,000-500,000 platelets per microliter (µL or 0.000001 liter). To obtain platelet-rich plasma, the patient’s blood is mixed with an anticoagulant and processed either manually by spinning it in a centrifuge to separate its components (centrifugation) or through an automated system. This processed fraction of the blood is termed “platelet-rich plasma.” With both the automated and manual processes the goal is to achieve the highest concentrations of platelets and remove the other components of the blood such as the red and white blood cells.
This fraction is then mixed with thrombin and calcium-chloride to activate the platelets before injection for therapeutic use. While both methods concentrate platelets, some are better than others in achieving high platelet concentrations with few white blood cells. The PRP used by the Veterinary Orthopedic & Sports Medicine Group (VOSM) is processed by the Regenerative Medicine Laboratory at the Leesburg, Virginia, campus of Virginia Tech, which uses a manual centrifugation method. This laboratory is able to yield platelet counts 7 to 10 times above normal, with few white blood cells present in the product.

This process concentrates the platelets as well as the growth factors, which is important in its clinical application because it theoretically amplifies the healing ability of the platelet. Growth factors work to promote healing by signaling cells to differentiate into specific tissue properties and then mature. So by treating with PRP at a specific site, it is postulated that healing will not only be hastened, but also the appropriate cells will be involved. Tissue healing is a complex process, and it has been difficult to define each factor’s role in healing. The advantage of PRP is that all of the growth factors are present in their normal ratio, virtually eliminating the need to determine how much of this or how much of that should be added to the “formula.”

Application

Platelet-rich plasma therapy is a minimally invasive treatment that can be used on an outpatient basis and generally does not require the patient to be anesthetized. First, 30-60 milliliters of blood is obtained from the jugular vein using a large gauge needle to avoid trauma to the platelets. The blood is then processed and prepared for injection. Once the PRP is processed, the area that is to be treated is clipped and aseptically prepared. Ultrasound guidance is used for injection accuracy since PRP is most effective when applied directly into the damaged tissue. It can be injected in a “peppering” manner to cover a wider area. Mild discomfort has been reported in people for 24-72 hours following the injection and can be managed with cold compresses and a synthetic opioid for pain relief. Minimal, if any, discomfort has been noted in horses and dogs following injection. Nonsteroidal anti-inflammatory medication and steroids are avoided during the post-injection period. Appropriate rehabilitation therapy is performed weekly for 8-12 weeks, depending on the diagnosed condition.

Clinical Applications of PRP

The field of human sports medicine has seen a particularly large surge of PRP use over the past decade. Tendon and ligament injuries account for nearly 45% of all musculoskeletal injuries in humans seen yearly in the U.S. Tendons and ligaments are susceptible to major stress dur-
ing sports, and if injured, heal slowly due to poor vascularity compared with other connective tissues. The rate of healing becomes increasingly more important when you have a complete disruption of a tendon or ligament, and primary surgical repair is warranted. The materials used to repair the torn tissue will eventually fail under normal cyclic loading if the body does not simultaneously repair itself in an appropriate time frame. Therefore, the concept of increasing the rate at which the body heals itself is incredibly attractive, as it will increase the odds of a successful surgical outcome (or potentially even eliminate the need for surgery). In the world of professional athletes, soft tissue injuries can result in a substantial set back in their careers. Consider the treatment of Hines Ward of the Pittsburgh Steelers. He received an injection of PRP two weeks before the 2009 Super Bowl for a grade II medial collateral injury of his knee. This therapy allowed Ward not only to play in the game, but also to contribute to the success of his team.

In veterinary medicine, the use of PRP in the clinical setting has been limited to a few studies and case reports documenting the use in horses and dogs. Its use in horses is commonplace as problematic tendon and ligament injuries are encountered frequently. Dogs can also suffer significant tendon and ligament injuries and PRP is now being considered both for treatment and for augmenting rehabilitation therapies. In our practice, we are currently using PRP in clinical studies for various tendon injuries, including biceps tendinopathy, supraspinatus tendinopathy, and Achilles tendon injury. In addition, the dog serves as an excellent model for multiple human conditions, thus there is an increasing interest in treating dogs with PRP to study the potential benefit in people. This should have an overwhelming impact on how we treat our canine patients in the future.

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Platelet-rich plasma is used in a variety of tissues and injuries in athletes of different species. PRP therapy will likely have a major role in the advancement of veterinary surgery and sports medicine over the next decade. The tissues most commonly treated currently include tendon and ligament, bone, and muscle. Deciding when to select PRP for use in these areas is complicated, as the biology of healing is complex and has many stages. The various tissues heal differently and the use of PRP may be found to be more beneficial in some tissues over others. Timing of its application may also be critical. In some areas, such as muscle, PRP may be best used when the injury is acute rather than more chronic. Thus far, the authors’ limited experiences in canine patients with tendon and ligamentous injuries have been promising. However, much work is needed to find the appropriate dose, time frame, and interval of injections before PRP therapy can be considered the standard of care.

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References