Regenerative Medicine in the Equine Athlete

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Introduction

Equine athletes of all disciplines are prone to musculoskeletal injuries. Unfortunately, many of the tissues at risk, including tendons, ligaments and cartilage, have limited intrinsic healing capabilities. Resultant repair tissue is often biomechanically inferior to native tissue leaving the animal prone to degeneration and re-injury. The goal of regenerative medicine is to “promote self-healing through endogenous recruitment or exogenous delivery of appropriate cells, biomolecules and supporting structures”,¹ such that the end product is a stronger tissue that more closely resembles native tissue. Currently, stem cell therapy, interleukin-1 receptor antagonist protein (IRAP), and platelet rich plasma (PRP) are the three main types of regenerative medicine used in equine musculoskeletal injuries. This seminar will focus on IRAP and PRP as stem cell therapy is covered in a separate seminar.

IRAP (Autologous conditioned serum)

Interleukin-1 receptor antagonist protein (IRAP) is an endogenous protein produced by immune cells, mainly monocytes. It is a competitive antagonist of interleukin-1 (IL-1), which is a central mediator of inflammation and degradation in joints. White blood cells can be stimulated to produce IRAP ex vivo such that serum with concentrated IRAP can be injected into inflamed joints. The final product is often referred to as autologous conditioned serum (ACS) as it contains other cytokines and growth factors beyond IRAP.² IRAP II (Arthrex Vet Systems) and Orthokine (Dechra Veterinary Products) are two commercially available products that rely on a 24 hour incubation of autologous blood in a specialized syringe that works to concentrate IRAP. Following incubation, the serum, which contains higher concentrations of IRAP, is drawn off in preparation for injection into the patient. Autologous conditioned serum can be aliquoted and stored at -20°C for future injections.

In horses, ACS is recommended for use in inflamed joints, including joints with synovitis, capsulitis, and osteoarthritis. A common treatment regimen would include treatment of the effected joint every 7-10 days for 3-5 treatments; however, many different treatment protocols exist. The volume of injection is extrapolated based on the size of the joint. At this time, ACS is only recommended for intra-articular administration as it has an unknown effect in tendons, ligaments, bursae and tendon sheaths. Few studies have been performed evaluating the effect of ACS; however, Frisbie et al. have demonstrated improved clinical outcomes in horses with experimentally-induced OA treated with ACS.³
Platelet Rich Plasma

Platelet rich plasma (PRP) is defined as a volume of plasma with a platelet count above that of whole blood, although the fold increase in platelet count is highly variable between different products. PRP can be prepared patient side following centrifugation or gravity filtration of autologous blood as platelets are smaller and less dense than RBCs and WBCs. Several commercial systems are available including ACP (Arthrex), GPS III (Biomet), Magellan (Medtronic), PRP-Equine (Harvest Tech); however, there is great variability in platelet and WBC concentration in the final products. The therapeutic effect of PRP is in large part due to degranulation of platelet α-granules. This leads to release of a milieu of growth factors including PDGF, TGF-β, FGF, VEGF, IGF-I, EGF etc. that help modulate the healing response in damaged tissue. PRP has been shown to promote healing by enhancing cell migration, proliferation and differentiation, improving matrix synthesis, and stimulating angiogenesis.4 Several equine experimental and clinical studies have found that PRP treated tendon and ligament lesions have improved strength and elasticity compared to control, and that re-injury rates are decreased.5–8

PRP is used most commonly to treat tendon and ligament lesions as it can be easily injected into core lesions under ultrasound guidance. Lesions can be treated in the acute phase when hypoechoic areas are present on ultrasound. PRP is prepared patient-side and then used to “fill” defects. Repeat injections can be performed at 3–4 week intervals. PRP is also being increasingly used to treat joint inflammation and osteoarthritis. Studies have shown that it is safe to inject into equine joints, with a minimal, transient increase in nucleated cell count noted following injection.9 PRP has also been shown to improve lameness scores in horses with naturally-occurring fetlock arthritis.10 Treatment of osteoarthritis with PRP may reduce some of the negative side effects of long-term intra-articular corticosteroid administration.

Pro-stride

Recently, Owl Manor introduced a new patient-side product available called Pro-Stride. It is an autologous protein solution that contains concentrated platelets and increased concentration of IRAP. The combination of growth factors from platelets and IRAP is suggested to have a combinatorial effect in the joint.11 In addition, the system does not require incubation; therefore, it can be used patient-side.

Amnion

Equine amnion-based products are available for treatment of wounds, ocular lesions, tendon/ligament injuries, and joints (AniCell Biotech, Chandler, AZ). Amnion is collected and decellularized such that an off-the-shelf bioscaffold is available. At this time, support for the use of amnion is mainly anecdotal.
**Conclusion**

Equine regenerative medicine is being used with increasing frequency and pre-clinical and clinical data continue to be promising. Many different therapies are available, with selection often dependent on the injury. Overall, regenerative therapies have the ability to improve the body’s natural healing ability such that a superior end product is produced.

**References**


