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Current Applications of Equine Regenerative Medicine

It's an exciting time in treating equine musculoskeletal injuries, said Laurie Goodrich, DVM, PhD, Dipl. ACVS. Regenerative medicine is opening doors to new and improved therapeutic options.

During a presentation at the 2015 World Equine Veterinary Association Congress, held Oct. 8-10 in Guadalajara, Mexico, Goodrich, an associate professor of surgery and lameness in the Department of Clinical Sciences and at the Orthopaedic Research Center at the Colorado State University College of Veterinary Medicine and Biomedical Sciences, reviewed three regenerative modalities—stem cells, PRP, and IRAP—with attendees.

Stem cells
Mesenchymal stem cells (MSCs) are derived from the adult horse's body, most commonly harvested from bone marrow or fat (adipose) tissue. Embryonic stem cells—those harvested from a foal's umbilical cord following birth, can also be used to aid tissue healing. Goodrich said stem cells are showing promise for treating a variety of injuries, including damaged cartilage, fractures, desmitis (ligament inflammation), and more.

Goodrich said both bone marrow- and adipose-derived MSCs can be beneficial, especially to tendon and ligament healing. But she noted that one study showed that bone marrow-derived cells have better ability to make the proteins needed in musculoskeletal tissue than adipose-derived cells.

While researchers are learning more about how MSCs function in horses, there are still many unknowns, including the exact mechanisms by which they improve tissue healing. Goodrich said. Researchers do know, however, that they have anti-inflammatory properties, influence cell-signaling factors, and orchestrate the formation of a tendonlike tissue matrix. Studies have shown that MSCs can survive for a wide time span, ranging from about 48 hours following administration to six weeks or so, she added.

Goodrich said at least 12 studies have found MSCs to have beneficial effects in the horse when it comes to helping tendons heal. She said some studies have even found that chronic suspensory desmitis can improve following stem cell administration.

Still, she added, scientists have yet to compare stem cells from different sources in a head-to-head manner.

There is less published research on MSCs impact on joint healing, but several studies have yielded good results when scientists have used the cells to treat meniscal disease, osteoarthritis, and cartilage damage.

"The effects of MSCs on various stages of joint disease is still under intense investigation, and clinical studies are forthcoming," she added.

Stem cells also carry a hefty price tag, making them cost-prohibitive for some owners.

Platelet-rich plasma (PRP)
Next, Goodrich turned her attention to PRP, which she noted has a lower price point than other regenerative therapies, making it a more appealing option for some owners. She cautioned, however, that researchers are still working to understand when, following injury, is the best time to administer PRP and where (directly into the lesion or to the surrounding areas, for instance) and how much to administer.

The smallest of all blood cells, platelets are found in blood and are responsible for the clotting mechanism. Platelets are the first responders to any injury. Essentially, PRP therapy delivers a high concentration of platelets in the form of blood plasma to a lesion, increasing the amount of growth factors at the site, to help the injury heal. The plasma is created by spinning whole blood down in a centrifuge, eliminating the red and white blood cells and leaving behind a high concentration of platelets.

Goodrich said *in vitro* (lab) studies have shown that PRP has the potential to improve collagen healing, vascularity, cellular metabolism, and histologic outcome. Researchers have also determined that the "if a little is good, more must be better" theory doesn't apply to PRP; administering a higher dose of platelets didn't improve collagen healing over smaller doses, she said.

Despite the existing laboratory research, there aren't many published clinical trials of PRP, she cautioned. One showed that horses treated with PRP healed significantly better than those not treated with PRP, while another showed no difference in racing success following PRP or other treatments.

She also relayed that PRP is most commonly used to treat soft tissue injuries. There's less evidence supporting its use in joints, and its efficacy there still needs to be proven, she said.

The bottom line, Goodrich said, is that PRP is safe and could help improve healing in soft tissue structures.

Interleukin-1 receptor antagonist protein (IRAP)
Finally, Goodrich touched on IRAP, which she said has evidence suggesting it has beneficial effects when used in horses' joints. Goodrich said IRAP tends to be a bit more expensive than PRP, but still less expensive than stem cells.

She explained that IRAP is made from white cells in the horse's bloodstream. Veterinarians collect blood from the horse and incubate it in the presence of specially designed glass beads, which amplify IRAP production. When the IRAP has reached the desired level, veterinarians can administer the substance to the injured horse.

Goodrich said IRAP has the ability to block interleukin-β-1 (a pro-inflammatory mediator) and reduce inflammation in joints, creating a healthier environment. And while there are only a few studies in horses, the ones that exist have yielded promising results. Researchers found that IRAP administration decreased both inflammation and lameness while increasing TGF-β (transforming growth factor-β) and IGF-1 (insulin-like growth factor) levels. Veterinarians have used both of these substances to promote cartilage and tendon healing.

Another perk: IRAP does not contain corticosteroids, making it a potential joint treatment option for horses at risk of developing laminitis following traditional intra-articular corticosteroid injections.

Goodrich added that while IRAP might also have benefits when used in injured tendons, there's currently no evidence to support that theory.