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Autologous Conditioned Serum Composition Evaluated

Joint disease: It's progressive, incurable, and widely prevalent among performance horses. Veterinarians can, however, provide affected horses with some relief in the form of conventional therapies, such as corticosteroids and/or hyaluronic acid injections or, in severe cases, biologic therapy. One such treatment is autologous conditioned serum (ACS), also called IRAP (interleukin-1 receptor antagonist protein).

At the 2015 American Association of Equine Practitioner's convention, held Dec. 5-9 in Las Vegas, Dane Tatarniuk, DVM, MS, clinical instructor in equine surgery and sports medicine at the University of Minnesota's College of Veterinary Medicine, in St. Paul, presented a study in which he and colleagues examined the composition of ACS—in particular an anti-inflammatory cytokine called the interleukin-1 receptor antagonist , or IL-1ra.

"There is prior evidence of this biologic therapy helping; however, the entire composition of ACS is unknown," he explained. "Prior research has focused predominately on IL-1ra, however many proteins (both anti-inflammatory and pro-inflammatory) may be present within the therapy."

But first, a little background on how ACS works. When a joint sustains injury, trauma stimulates the release of inflammatory proteins within the joint including IL-1 and other cytokines (proteins that signal cells to move toward inflammation sites). These accelerate and worsen inflammation, contributing to cartilage degradation that leads to an overall downward spiral of joint degeneration.

The objective in using ACS is to block the activity of interleukin-1 on joint tissues and slow osteoarthritis progression. To obtain ACS, the veterinarian draws blood from the horse and incubates it for 24 hours in a syringe with borosilicate beads that stimulate IRAP production. Centrifuging the blood at this point removes IRAP-containing serum from the blood cells for immediate injection back into the joint or freezing for future use.

In the study Tatarniuk described, he and colleagues selected 11 horses with confirmed coffin joint arthritis and administered ACS as three injections spaced seven days apart: Day 0, 7, and 14. He said the ACS therapy was compared to two control groups: one which had no exposure to beads or incubation, and another that had no exposure to beads but was incubated for the same duration as the ACS therapy. Synovial fluid samples collected at Day 7, 14, and 21, and compared back to a baseline synovial fluid sample originally taken from each horse that was treated on Day 0 (prior to any ACS treatment).

"Following ACS administration, IL-1ra (the main protein that is advocated as effective in the product) was unchanged in synovial fluid samples ... as compared to the baseline prior to treatment," Tatarniuk said.

He said he isn't sure why there was no change, but his team has several hypothesis, including:

- The IL-1ra protein is highly actively bound to the IL-1 receptor. Therefore there was no increase in concentration within synovial fluid found when synovial fluid was sampled seven days following treatment, or
- Potentially, the IL-1ra protein is degraded, absorbed, or metabolized out of the joint within the seven day timeframe.

"This is an important consideration, as if the therapy is only staying in the joint for a very transient time, then it may have implications for its effectiveness as a therapeutic," Tatarniuk said.

More research is needed to confirm the actual cause of this finding, he added.

The number of needle sticks in the joint or the presence of blood contamination had no effect on the results. Interestingly, he said, there were no changes in lameness scores throughout the 21 days. When evaluating IL-1ra concentrations in ACS compared to control serum groups, ACS was different from regular serum but not different compared to the incubated control group.

Tatarniuk said the team's results were two-fold. "The concentrations within the ACS product (serum) show that ACS increased only when compared to the unconditioned, unincubated control group," he explained. "This is important (because) ACS is highly advertised as requiring borosilicate beads to increase IL-1ra. However, it appears from our findings that incubation alone may also result in comparable concentrations. This statement only holds true when looking at IL-1ra concentrations alone."

Secondly, "when looking at all biomarkers (other proteins than IL-1ra) there still is a difference between ACS and incubated, unconditioned serum—to be specific, decrease levels of IL-4, IL-6, IL-8 and increase levels of IGF-1)," he continued. "So, we can't entirely state that ACS is exactly the same as incubated serum without exposure to beads, when considering the global concentration of proteins (or, the biomarkers)."