Proceedings of the 12th International Congress of the World Equine Veterinary Association 
WEVA

November 2 - 5, 2011 
Hyderabad, India
Therapies that are injected intralesionally are usually directed at healing tendons or ligaments. They are most often intended to augment the healing processes locally by providing the necessary components of healing to the tissue being treated. Alternatively they may act locally to either reduce inflammation and/or signal the cellular and molecular components of the injured and surrounding tissues to begin the reparative processes. During repair of these tissues, injured elastic fibers are replaced with modified fibrous scar tissue, resulting in repair that is suboptimal. The quality of the repair varies greatly depending on the severity of the lesion, the inherent healing properties of the individual, the rehabilitation program, and the local environment of the lesion. Some injuries may repair and resolve with enough mature collagen so that they return to normal size, with sufficient remodeling that results in parallel alignment of the fibers within the tissue. Other injuries form a scar, with a resulting increase in size of the tendon/ligament, poor or random fibrous tissue alignment, and peritendinous/ligament fibrosis.

Intralesional approaches are directed at maximizing the chances for a more physiologically functioning tendon. Along with intralesional therapies, rehabilitation and constant ultrasonographic monitoring must accompany any treatment. Treatments usually reduce the acute inflammatory response and hemorrhage in the acute phase and improve fiber alignment during reparative phase. Ultimately, the goal is to maximize the chances for a tendon or ligament to repair with adequate strength and elasticity for a return to a similar level of performance with minimal risk for re-injury.

Mesenchymal stem cell (MSC) therapy in veterinary orthopedics has generated much enthusiasm in the last decade. Various uses have been described including treatment of subchondral bone cysts, bone fracture repair, and cartilage repair. (Kraus, Kirker-head, 2006) (Nixon, et all, 2000) However, by far the most frequent use of mesenchymal stem cells has been in treatment of overstrain-induced injuries of tendons in horses. (Richardson, et all, 2007)

Although the mechanism of action in how these cells influence their “trophic” activity is still under intense investigation, many models of animal studies suggest that MSCs secrete bioactive molecules that: a) inhibit apoptosis and limit the field of damage or injury, b) inhibit fibrosis or scarring at the sites of injury, c) stimulate angiogenesis and bring in a new blood supply, and d) stimulate the mitosis of site tissue-specific and tissue-intrinsic progenitor cells. (Kaplan, 2009) In racehorses, the reinjury rate in tendons sustaining SDF tendonitis is approximately 56%. (Dyson, 2000) Due to scar tissue formation, the primary need to restore functionality has encouraged development of regeneration strategies. Regenerative strategies require an exogenous cell source. Tendons and ligaments do not have a lack of cellular inflammation following injury however; cells actually involved in the synthesis of new tissues are mostly locally derived. Transplantation of MSCs into various injured skeletal tissues has been shown to promote healing and the use of
autologous cells has a benefit since they do not incite an immune response from the host. (Caplan AI, et all,1993) (Ferrari, 1998) (Hildebrand, 2002). Current theories on how transplanted cells act in tendon when injected intrathecally are that they either differentiate into cells capable of synthesizing tendon matrix or they secrete important factors which induce adjacent cells to synthesize tendon matrix. (Richardson, 2007)

Currently, two techniques exist for MSC transplantation using intrathecal injections. One has used non-adipocyte-cell mixture from fat, and the second has used cultured bone marrow aspirate. The fat-derived stem cells do not involve a culture step and therefore have the advantage of cheaper cost and speed of preparation (cells returned to the practitioner within 48 hours). However, the cell mixture is believed to be heterogenous with regards to cell type. A recent small controlled study using adipose-derived cells in collagenase model of tendon injury reported some benefit in terms of crymp pattern. (Del Bue, 2008) Another study reported a return to athleticism of 14 out of 16 horses with SDF tendonitis with no comment on re-injury rate. (Nixon, 2008). However; larger scale clinical data are lacking.

The bone marrow derived MSC technique involves aspirating bone marrow from the sternum or tuber coxae, transferring to a laboratory for culture and expansion and then implanting the cell population (approximately 10-50 x 10^6) under ultrasound guidance. (Goodrich, 2008) This technique has been widely used in the US, UK, Europe, and Australia. Currently, long-term follow up is encouraging. Over 168 race horses undergoing this regime have been followed. (Smith, 2008) For horses that have returned to work, only 18% have re-injured. This is in contrast to a 56% reinjury rate for horses receiving no intralesional therapy. No adverse effects were reported other than ultrasonographic evidence of needle tracks. Two smaller scale studies, one in research horses (Schnabel, 2009) and one in 11 race horses (Pacini, 2007), also reported improved tendon repair. Although current data are encouraging in this area, large scale clinical trials that compare untreated horses to treated horses are needed.
WEVA Congress References


