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Regenerative Medicine and Rehabilitation for Tendinous and Ligamentous Injuries in Sport Horses

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KEYWORDS

- Tendonitis Desmitis Regenerative medicine Rehabilitation Stem cell
- Platelet-rich plasma

KEY POINTS

- Tendon and ligament injuries are common in athletic horses.
- Spontaneous healing of tendon and ligaments occurs; however, repair tissue is usually biomechanically inferior leading to high reinjury rates.
- Regenerative medicine therapies have been used with increasing frequency to improve the quality of repair tissue.
- Regenerative medicine therapies including stem cell therapy, platelet-rich plasma, and autologous conditioned serum lead to improved repair of tendon and ligament lesions.
- A tailored rehabilitation program, including controlled exercise and adjunctive treatments, is also key to success in cases of tendonitis and desmitis.

INTRODUCTION

Tendon and ligament injuries are common in all sports horses, with specific injuries being overrepresented in certain disciplines. Most tendon and ligament injuries are categorized as overstrain injuries, especially in racehorses where tendons are operating close to their functional limits. Tendons and ligaments are highly organized tissues that depend on the strength and structure of the extracellular matrix (ECM) to function. Overloading can lead to physical damage and degeneration. If peak loads on a tendon or ligament are greater than the structural strength, fibrillar slippage, breakage of cross-linking, fibrillary rupture, and tendon tearing can occur. Although tendons and ligaments have the ability to spontaneously heal with time, the scar tissue that

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Vet Clin Equine ■ (2018) ■-■ https://doi.org/10.1016/j.cveq.2018.04.012 0749-0739/18/© 2018 Elsevier Inc. All rights reserved. fills lesions is biomechanically inferior leading to high reinjury rates and recurrent lameness.

The therapeutic objective for horses with tendonitis and/or desmitis is to return the horse to its previous athletic level and prevent reinjury. Rehabilitation has been a mainstay of therapy following tendon and ligament injuries. More recently, regenerative medicine has been used to "promote self-healing through endogenous recruitment or exogenous delivery of appropriate cells, biomolecules and supporting structures," such that the healed product more closely resembles native tissue. Restoration of normal biomechanical function and structure would allow horses to perform at previous athletic levels with reduced risk of reinjury. 5,6

The goal of regenerative medicine is to restore normal structure and function of injured tissues, with the three main components of regenerative medicine including scaffolds, cells, and bioactive signals. Stem cell therapy, platelet-rich plasma (PRP), and autologous conditioned serum or plasma are the main orthobiologic products currently used in equine musculoskeletal injuries, although growth factor therapy and amnion are occasionally used. All of these injectable orthobiologic therapies can be used in the treatment of superficial digital flexor (SDF) tendonitis, proximal suspensory desmitis, suspensory branch desmitis, and various other tendon and ligament injuries. Acute, subacute, or chronic tendinitis/desmitis with hypoechoic areas noted on ultrasonographic examination are amenable to intralesional injection. Through slightly different mechanisms, the previously mentioned therapies work to modulate the inflammatory process and regulate tissue repair. Combined with controlled rehabilitation, regenerative medicine has become an important treatment option for horses with tendon and ligament lesions.

REGENERATIVE MEDICINE Growth Factor Therapy

Treatment of tendon and ligament lesions with several different growth factors has been reported. Growth factors are used to stimulate cellular differentiation, angiogenesis, and ECM synthesis. The beneficial effects of insulin-like growth factor (IGF)-I^{7,8} and platelet-derived growth factor⁹ have been demonstrated in equine tendons. IGF was shown to improve the ultrasonographic appearance of SDF tendon (SDFT) and decrease swelling following intralesional injection in an equine collagenase-induced tendonitis model. When used in horses with naturally occurring SDF tendonitis, IGF-I was associated with improved ultrasonographic appearance of lesions; however, treatment carried only a moderate prognosis for return to racing (62%) with a moderate rate of reinjury (46%).8 Conversely, intramuscular injection of recombinant equine growth factor was found to have significant negative effects on healing in a collagenase-induced SDF tendonitis model. 10 One major downfall of the growth factor approach, is the limited number of growth factors that can be injected at one time. More recently, the concentrated milieu of growth factors in PRP has been exploited as high concentrations of numerous growth factors are simultaneously administered.

Platelet-Rich Plasma Therapy

PRP is defined as a volume of plasma with a platelet count greater than that of whole blood, although the fold increase in platelet count is highly variable between different products. 11 The therapeutic effect of PRP is in large part caused by degranulation of platelet α -granules. 12 Degranulation leads to release of a milieu of growth factors including PDGT, transforming growth factor- β , fibroblast growth factor, vascular

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