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Εναλλακτική θεραπευτική προσέγγιση της συνδεσμίτιδας στην έκφυση του συνδέσμου αναρτήρα του κυνήποδα σε οπίσθιο áκρο: αναδρομική μελέτη σε επτά áλογα

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■ Alternative treatment for proximal suspensory desmitis in the hind limb: retrospective study in seven horses

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■ Εναλλακτική θεραπευτική προσέγγιση της συνδεσμίτιδας στην έκφυση του συνδέσμου αναρτήρα του κυνήποδα σε οπίσθιο άκρο: αναδρομική μελέτη σε επτά άλογα

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ABSTRACT. Proximal suspensory desmitis (PSD) has become a frequently diagnosed condition commonly affecting athletic horses. In this study, seven horses with PSD in a pelvic limb were included. Definitive diagnosis was based on clinical signs, results of local anesthesia and ultrasonographic and radiographic examination. Following the initial anti-inflammatory treatment, PSD was treated with an alternative, minimally invasive method, including series of periligamentous injections containing mepivacaine hydrochloride, heparin sodium, a preparation containing natural ingredients and deproteinised haemoderivative of calf blood. Depending on the severity of each case, all horses returned to full work after 8 to 12 weeks.

Keywords: hindlimb, horse, proximal suspensory desmitis

ΠΕΡΙΛΗΨΗ. Η συνδεσμίτιδα στην έκφυση του συνδέσμου αναρτήρα του κυνήποδα αποτελεί μια σχετικά συχνή πάθηση, η οποία προσβάλλει κυρίως ίππους αθλητικής υπασίας. Στη μελέτη αυτή συμπεριλήφθηκαν επτά ίπποι με συνδεσμίτιδα της έκφυσης του συνδέσμου αναρτήρα του κυνήποδα ενός εκ των οπίσθιων άκρων. Η τελική διάγνωση έγινε με βάση την κλινική εικόνα του ίππου, την περιφερική αναισθησία, καθώς και τον υπερηχογραφικό και ακτινολογικό έλεγχο. Η θεραπεία περιελάμβανε μετά την αρχική χορήγηση μη στεροειδών αντιφλεγμονώδων φαρμάκων και την εφαρμογή μιας σειράς περιτενόντιων εγχύσεων που αποτελούνταν από υδροχλωρική μεπιβακαΐνη, νατριούχο ηπαρίνη, ένα σύνθετο ομοιοπαθητικό και παράγωγο αίματος μόσχου. Το σύνολο των ίππων ανταποκρίθηκε με επιτυχία στο θεραπευτικό πρωτόκολλο και επανήλθε πλήρως στην αθλητική δραστηριότητα σε διάστημα 8 έως 12 εβδομάδων.

Λέξεις ενρετηρίασης: ίππος, οπίσθιο άκρο, συνδεσμίτιδα του συνδέσμου αναρτήρα του κυνήποδα

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INTRODUCTION

The suspensory ligament, also known as interosseous medius muscle, is a tendinous band containing a variable amount of muscular tissue (2-11%) (Dyson, 1998). Injuries to the suspensory ligament can be categorized as follows: (i) lesions confined to the proximal third (proximal suspensory desmitis), (ii) lesions of the middle third (body lesions) and (iii) lesions of the medial and/or lateral branch (branch lesions) (Bertone, 2011). The area of origin of the suspensory ligament on the proximal palmar/plantar aspect of metacarpal/metatarsal bone III is of great importance since proximal suspensory desmitis (PSD) is a common soft tissue injury in athletic horses. Mature sport horses 4- to 10-year-old (Dyson, 1991; 1994), young racing Thoroughbreds (Pilsworth, 2002), endurance horses (Dyson, 1998) and dressage horses (Murray et al., 2006; Dyson and Genovese, 2010) are particularly at risk of injury.

PSD of the forelimb is an insertion desmopathy (Marks, 1999). Lameness varies from mild to moderate and rarely severe, especially when lesions involve the enthesis. Acute injuries may be accompanied by slight edema, localized heat, pain on digital pressure and positive response to flexion test. Box rest and controlled exercise may provide a propitious response without recurrent injuries, although chronic cases require more prolonged rehabilitation (Dyson, 2000).

In contrast to the forelimb, PSD on the hindlimb has generally a poor prognosis (Dyson, 1994). Persistent or recurrent lameness is frequently reported, despite prolonged periods of rest and controlled exercise. This is probably associated with a compartment-like syndrome and compression of the adjacent plantar metatarsal nerves (Dyson, 2007; Toth et al., 2008). Bilateral lesions occur more frequently in the hindlimbs than in the forelimbs (Dyson, 2007). Predisposing factors include straight hock conformation, hyperextension of the metatarsophalangeal joint and long toe-low heel conformation (Dyson, 2007). Lameness can vary from subtle, resulting in poor performance and stiffness, to severe. In acute cases there may be edematous swelling and localized heat but usually there are no detectable clinical signs suggestive of the origin of pain (Dyson, 2007). According to

the literature mentioned above, PSD on the hindlimb is associated with a guarded to poor prognosis.

Current treatment options for PSD include platelet rich plasma (Waselau et al., 2008), autologous conditioned serum or interleucin receptor antagonist protein (Rindermann et al., 2010; Wehling et al., 2007), mesenchymal stem cell therapy (Smith, 2008), acellular urinary bladder matrix (Mitchell, 2006) and extracorporeal shockwave therapy (Crowe et al., 2002). Although scientific evidence support the efficacy of these methods, they cannot be used on all horses because of financial constraints.

The aim of this study was to investigate the potential use of periligamentous injections containing mepivacaine hydrochloride (Mepivacaine injection 2%®), heparin sodium (Heparin®, LEO), a homeopathic preparation (Traumeel®) containing plant extracts and a deproteinised haemoderivative of calf blood (Actovegin®) in horses with PSD, as an alternative, whenever the aforementioned methods were not available.

CASE DESCRIPTION

Presentation of cases

In this study, seven horses with moderate to severe proximal suspensory desmitis were selected for this treatment protocol. Most of the horses were sport horses, particularly used for dressage or show jumping. Breeds included Warmbloods (4), Thoroughbreds (2) and one Thoroughbred cross. Horses were presented either with a history of acute (3) or chronic lameness (4). The initial diagnosis had been based on clinical examination, perineural anesthesia and findings of radiological and ultrasonographic examination.

A clinical examination and thorough lameness evaluation occurred to determine the cause of lameness. Horses were evaluated at walk, trot in hand on a straight line and lunged on hard and soft ground. Lameness was graded on a scale of 0 to 5, according to American Association of Equine Practitioners grading system. Seven horses with unilateral hind limb lameness were selected. Three of these horses

presented with acute lameness, a slight swelling in the proximal metatarsal region, localized heat and mild pain upon palpation. The degree of lameness ranged from 1 to 3. Trotting in straight line on soft ground intensified low-grade lameness. Full and distal limb flexion tests were performed. Full limb flexion tests were positive in 6 out of 7 horses.

In order to localise the site of pain, perineural anesthesia with mepivacaine hydrochloride was performed on the lame limb. Six-point-nerve blocks, followed by subtarsal and tibial nerve blocks in all horses were performed with the limb bearing weight. In five animals, lameness retreated following a subtarsal block. Lameness in two animals was substantially improved only after anesthetising the tibial nerves.

A thorough radiographic examination was carried out in all cases to exclude any other possible lesions. Radiographic examination of the proximal metatarsal region included the lateromedial, dorso-plantar, dorsolateral/plantaromedial oblique and dorso-medial-plantarolateral oblique views. In two animals, there were no detectable radiographic abnormalities. Radiographic lesions were identified in five horses (four with chronic lameness and one with acute presentation), including sclerosis of the trabecular pattern (3/5), enthesophyte formation (3/5) and osteolysis in the proximal aspect of the third metatarsal bone (5/5).

Horses were categorised according to the severity of clinical signs in conjunction with ultrasonographic abnormalities. Ultrasonographic examination of the plantar metatarsal region with a 10 MHz linear transducer was followed to document and specify the type of injury. Longitudinal and transverse views were performed including the proximal aspect, the body and the branches of the suspensory ligament. Ultrasonographic abnormalities included enlargement of the cross-sectional area (7/7), poor definition of margins (7/7), hypoechoic or anechoic core lesions or diffuse reduction in echogenicity (7/7), ectopic fibrosis or mineralization (2/7), poor fiber alignment, reduction of space between the suspensory ligament and the palmar cortex of the third metatarsal bone (7/7).

Cross-sectional area size of the ligament was evaluated. Based on ultrasonographic evaluation,

only cases with mild to severe core lesions, from 30% to 50% of the cross sectional area, were included for the treatment protocol. As mentioned before, only seven animals met the criteria for inclusion in this study. In one horse with acute lameness, with subtle ultrasonographic abnormalities, evaluation was repeated after ten days.

Initially, all horses with acute or recurrent lameness received conservative treatment with non-steroid anti-inflammatory drugs, including phenylbutazone (dose rate: 4.4 mg kg⁻¹ bw iv sid) (Phenylbutazone injection[®]), ketoprofen (dose rate: 2.2 mg kg⁻¹ bw iv sid) (Romefen 10% inj[®]) or flunixin meglumine (dose rate: 1.1 mg kg⁻¹ bw iv sid) (Finixin[®]). These drugs were administered for 7 to 10 days, prior to periligamentous injections.

Following anti-inflammatory therapy, periligamentous injections with Mepivacaine injection[®] 2% (5 mL), Heparin[®] (5 mL), Traumeel[®] (5 mL) and Actovegin[®] (5 mL), both on the medial and lateral aspect were performed. The treatment regimen included one injection repeated four times at 7-day intervals. A thin layer of heparin gel (Hemeran[®] gel) and pressure bandage were applied to each injection site. Heparin gel was applied for 4 days, during which time horses were restricted to box rest. Following that period horses were hand-walked for 10 minutes twice a day for three days. After six weeks of treatment, horses were gradually put back into exercise.

Outcome

The treatment protocol described above had positive results in all cases. Clinical examination and locomotion evaluation were carried out at walk and trot eight weeks after initial evaluation. The majority of horses (6/7) showed no detectable gait abnormalities. One horse was still lame (1/5) at that time. Clinical assessment was repeated to all horses after 12 weeks, before resumption to intense training, revealing no signs of pain or lameness.

Ultrasonographic re-evaluation revealed restoration of the normal anatomic size, normal fibre alignment and marked improvement in echogenicity and fibre pattern in 6/7 cases, whereas, hypoechoogenicity

and slightly enlargement of cross-sectional area was detected in one case. Three months after treatment, ultrasound examination revealed normal fibrillar architecture and complete recovery in all seven horses.

In conclusion, all horses were sound and resumed full work 12 weeks after initial examination despite the guarded prognosis. All horses remained sound for at least 12 months after the initial presentation.

DISCUSSION

In proximal suspensory desmitis, lameness may occur in forelimbs or hindlimbs, unilaterally or bilaterally, although a significantly better prognosis for athletic return and future soundness is expected if forelimbs are affected (Dyson, 1991). In horses with acute lameness, localised clinical signs may be absent. In this study, initial clinical evaluation was followed by a number of diagnostic methods to establish final diagnosis. Subtarsal perineural analgesia of plantar and plantar metatarsal nerves did not eliminate lameness in two hindlimbs. Lack of lameness improvement may be due to the fact that infiltration is often performed too distally (Bertone, 2011). Two horses were subjected to tibial nerve blocks showing significant improvement.

The aim of conservative treatment with non-steroid anti-inflammatory drugs was to suppress the inflammatory response prior to periligamentous injections. The alternative treatment protocol applied in this study was based on Dr. Mueller-Wohlfahrt's Actovegin® injection regime, developed to treat muscle injuries in professional athletes (Orchard et al., 2008). Actovegin®, a deproteinised serum extract of bovine origin, is thought to improve the transport of glucose over a plasma membrane and the uptake of oxygen by tissues (Nordvik, 2002). This could lead to aerobic oxidation, providing a cell with access to more energy and potentially an enhanced function (Nordvik, 2002). Actovegin contains large amounts of superoxide dismutase enzymes and magnesium, thus protecting the cell from superoxide toxicity (Gardner et al., 1995; Heinrich et al., 2006; Lee et al., 2011).

Although the pharmakocinetic effect of Actovegin® is not fully comprehended, preclinical data suggest its neuroprotective and anti-oxidative action (Martin et al., 2011). A study by Astashkin et al. (2013) also indicates that Actovegin® reduces the spontaneous formation of oxygen radicals by blood phagocytes and possibly inhibits the development of chronic inflammation determined by heart failure and systemic hypoxia. Studies in rats show that Actovegin® produces a significant development of bundles of collagen fibers (Antonova, 2008).

Clinical trials demonstrated the ability of Actovegin® to improve the quality and decrease the rehabilitation period after a muscle injury (Lee et al., 2011). Another plausible explanation for the beneficiary effect of Actovegin® in this case series is that the suspensory ligament consists of a variable amount of muscular tissue especially at its proximal part. Although, more research is needed in order to understand and prove the mechanism of action of Actovegin®, it seems that it does enhance healing in muscular, tendinous and ligamentous injuries. Previous reports (Dyson, 2007) claim that they did not manage to statistically prove a correlation between enhanced healing and administration of Actovegin®. Unfortunately, treatment protocol and the potential reason of failure are not presented. Presumably, the difference in results can be explained by the composition of the therapeutic formula or the frequency and the number of intervals. At this stage it might be worth mentioning that an effort was made to perform the injection as close as possible to the lesion. Although the number of cases in this study is limited, it seems that the treatment regime based on a combination of ingredients led to marked improvement.

The rationale of using Traumeel® in this study is supported by evidence suggesting the inhibitory role in pro-inflammatory mediators from immune cells (Porozov et al., 2004), the synergistic action of the ingredients and the acceleration of the healing process (Lussignoli et al., 1999). It has been shown that between dilutions of 10^{-1} to 10^{-7} , Traumeel® has a selective inhibitory effect on some pro-inflammatory mediators, such as IL-1 β , TNF α , and IL-8 (Porozov

et al., 2004). A recent controlled trial involving 449 adults with ankle sprain also determines the efficacy of Traumeel compared with other inflammatory substance (de Vega et al., 2013).

Heparin, beyond its well established anti-coagulant effect, may possess anti-inflammatory properties. In this study, heparin was used, because of its potential ability to improve microcirculation (Incandela et al., 2001), limit the excessive swelling and haematoma (Dragani et al., 1989) and reduce pain (Cosimo et al., 2011). Recently, Alkhamesi and Schlachta (2013) indicated the anti-adhesive effect of heparin post-operatively in an animal model. Although continuous, daily injections with low-molecular heparin found to delay tendon healing (Virchenko et al., 2008), in this trial Heparin® was administered in 7-day intervals, in order to overcome this adverse effect, in an effort to decrease adhesion formation.

Local anesthetics are commonly used in conjunction with corticosteroids or other agents, in order to reduce pain, as well as to promote an adequate dispersion of the main drug. Mepivacaine was added in the treatment regime as a widely used local anesthetic agent carrying minor toxicity risk (Kasaba et al. 2003; Park et al., 2011).

Interestingly, in this study periligamentous injections have given a favorable response. All horses have returned to full work exercise and soundness within 12 weeks. Horses with chronic lesions needed a prolonged recovery period, confirming the current data (Dyson, 2007), although, they presented a better outcome than expected, probably due to local treatment in a timely manner.

Recently, platelet rich plasma (PRP) has been described as a novel therapy in the treatment of proximal suspensory desmitis either in human or equine athletes. PRP is an autologous concentrate of blood cells, playing a crucial role in tissue healing by delivering growth factors to the site of injury. A study resulted that injection of PRP in 9 Standardbred horses provided a fair outcome (Waselau et al., 2008). Another study concluded that PRP increases metabolic activity and advances maturation of repair tissue in experimentally induced core lesions in superficial

digital flexor tendons (Bosch et al., 2010). Injection of bone marrow has been described for PSD injuries, with promising results (Herthel, 2001). Compressive damage to the deep branch of the lateral plantar nerve in hindlimb proximal suspensory desmitis can confound persistent lameness, while neurectomy of the same nerve resolves lameness by interrupting the sensory innervations (Tóth et al., 2008). Local injection with urinary bladder matrix has resulted in 44% of 77 horses with PSD to full work resumption (Mitchell, 2006). Extracorporeal shockwave therapy is frequently used in treatment of equine tendinopathies, aimed to improve the quality and speed of tendon healing. However, some authors question its safety, reporting adverse side effects (Costa et al., 2005; Diakakis et al., 2005).

CONCLUDING REMARKS

The aim of this paper was to indicate that, in the absence of the elaborate techniques described above conservative therapy in conjunction with a standardized regimen of periligamentous injections also provided a fair outcome. Despite the lack of a control group and the small number of cases, based on the satisfactory clinical response the suggested alternative regimen may be a preferable regimen considering the relatively low cost and practicality. All horses responded fully to stall rest and anti-inflammatory therapy combined with standardized regime of periligamentous injections, considering the resumption to work and ultrasonographic follow-up. According to the progress of cases described above it is concluded that periligamentous injections with homeopathic solutions in a standardized regime may be used as a promising alternative treatment for PSD.

CONFLICT OF INTEREST STATEMENT

The authors of this paper certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript. ■

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