

Treatment of Tendon and Ligament Injuries with UBM Powder

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Take Home Message

UBM Powder^a derived from SPF pig urinary bladder is proving to be very useful tool in the treatment of tendon and ligament injury. Convalescence is reduced and quality of healing appears to be superior to natural processes.

Introduction

Recent work in human and veterinary medicine using growth stimulants, bone marrow implants and stem cells have stirred interest in regenerative medicine as a technique for tissue repair. Extracellular matrix or ECM has been tested and proposed as an agent for tissue reconstruction.¹ ECM's have been derived from several tissues including the submucosa of pig small intestine and urinary bladder. The objective of this retrospective study was to assess the therapeutic value of Urinary Bladder Matrix Powder (UBM) for tissue regeneration and return to function in tendon and ligament injuries of the equine limb. Assessment of response was by review of lameness evaluation, physical characteristics of involved structures, and visible improvement of identified ultrasound lesions in affected structures.

Materials and Methods

A total of 190 lesions of affected equine suspensory ligaments and tendons were treated during the period from April 1, 2002 to June 15, 2005. Suspensory ligament lesions included injuries to the proximal suspensory ligament, suspensory body, and branches. Tendon injuries included superficial and deep flexor tendons and the gastrocnemius tendon. Two inferior check ligaments were also included in the review.

Treated horses were initially presented for evaluation of lameness of presumed suspensory ligament or tendon origin. The origin of lameness was confirmed by a variable combination of palpation, lameness score assessment, diagnostic nerve blocks, nuclear scintigraphy, and, in all cases, diagnostic ultrasound.²

Treatment was accomplished by intra-lesional injection of 0.2-0.4 grams of UBM powder suspended in 6-10 ml of normal saline^b. All horses treated after August 1, 2003 received no more than 0.2 grams UBM suspended in 6 ml saline for any one specific lesion. Injection was performed after ultrasound examination determined the location of the injured tissue. Proximal suspensory lesions of the forelimb (and the two inferior check ligaments) were injected percutaneously with the exception of two cases that were performed via a proximal metacarpal fasciotomy. All proximal suspensory lesions of the hind limb were injected through a proximal metatarsal fasciotomy incision with the exception of three cases. Suspensory branch and superficial flexor lesions were treated percutaneously. The one deep digital flexor lesion was treated intra-operatively during an annular ligament desmotomy. The gastrocnemius lesion was treated with ultrasound guidance. A thorough surgical prep was performed regardless of the

^a ACell Vet™, UBM Powder, ACell, Inc., Jessup, MD

^b Saline Solution, 0.9%, Phoenix Pharmaceutical, St. Joseph, MO 64503

subsequent procedure. All percutaneous injections were performed under standing sedation using detomidine^c and butorphanol^d and a nose twitch. Regional anesthesia was used only with those horses that remained sensitive to needle puncture. All surgical cases were anesthetized with a combination of diazepam^e, xylazine^f, and ketamine^g and maintained with halothane^h. In all proximal suspensory cases a 20 gauge, 1 ½ inch needle was used to distribute the suspension through the tissue. All suspensory branch lesions and all superficial digital flexor lesions were injected percutaneously with a 23 gauge, ¾ inch needle. The one gastrocnemius tendon was injected percutaneously using ultrasound guidance with a 20 gauge, 1 ½ inch needle.

Proximal suspensory ligament lesions were injected via one location using a “fanning” technique throughout the substance of the ligament in the region of injury. In the case of percutaneous injections this was accomplished from the lateral aspect of the limb just distal to the head of the fourth metacarpal/metatarsal bone. Suspensory branches and superficial digital flexor tendons were injected at multiple sites in the lesion at approximately one centimeter intervals. Approximately 1 -1.5 ml of suspension was used per injection site. While 0.2 grams UBM powder was most often used, up to 0.4 grams was used in some therapies per limb prior to Aug 1, 2003. The greater quantity was judged to be more than necessary with experience in using the product. If more than one limb was involved, routinely 0.4 grams UBM was used.

Following injection therapy, all non-surgical cases were placed in a sterile bandage for 2-4 hours. The bandage was removed and the limb was iced for 30 minutes around the affected area. This was performed q12h for 3 days. A dry wrap was used during the day and a moist “clay” poultice under paper was applied over night for 3 consecutive days. Surgically treated horses underwent bandage changes initially every 2 days for 2 changes, then every 3 days until suture removal. Surgically treated horses were given 15 grams trimethoprim/sulfadiazine pasteⁱ once daily for 5 days as prophylaxis. All treated horses received an injection of 500mg flunixin meglumine^j intravenously at the time of treatment and continued on 250 mg flunixin meglumine, q12h, orally for a total of five days.

Twice daily hand walking was begun on the day following injection. Even if the horse was uncomfortable, activity was encouraged. Hand walking continued on an increasing basis for thirty days. From August 2003 through January 2004, all cases (if available) underwent an ultrasound examination at 5 days post-treatment to assess post-injection response. Activity was normally increased after ultrasound evaluation at thirty days. More chronic lesions of the suspensory origin and body were started at walk/trot work after thirty days in most non-surgical cases. Newer injuries continued to walk another thirty days but often did so under saddle. All injection cases were walking and jogging to a limited extent after 60 days, however surgical cases were restricted to walking or a round pen for 120 days. Surgical cases were returned to work after 120 days walking/rest.

All horses receiving therapy underwent ultrasound examination prior to treatment and were then re-examined periodically to assess progress, typically at 30, 60, 90 and 120 days.³ A limited number of horses were examined at five days post injection to assess injection response.

^c Dormosedan, Pfizer Animal Health, NY, NY 10017

^d Torbugesic, Fort Dodge Animal Health, Fort Dodge, Iowa 50501

^e Diazepam Injection, Abbot Laboratories, North Chicago, IL 60064

^f Xyla-Ject, Phoenix Pharmaceutical, St. Joseph, MO 64503

^g Ketaset, Fort Dodge Animal Health, Fort Dodge, Iowa 50501

^h Halothane, Halocarbon Laboratories, River Edge, NJ

ⁱ Tribissen ® 400 Oral Paste, Schering-Plough Animal Health, Union, NJ

^j Banamine, Schering-Plough Animal Health, Union, NJ

Improvement in lesion grades and soundness jogging in hand were assessed at all examinations performed thirty days or greater post treatment. A review of response to therapy was performed on all horses that were deemed to be twelve months or greater post-treatment at the time of this writing.

Results

A total of 190 lesions were treated with UBM powder. One hundred and twenty-nine proximal suspensory and suspensory body lesions were treated; 75 hind limb suspensory lesions and 54 forelimb suspensory lesions. A total of 75 suspensory lesions were treated using fasciotomy. Thirty-two suspensory branch lesions and 25 superficial digital flexor tendon lesions were treated. Additionally, two lesions of forelimb inferior check ligaments, one deep digital flexor tendon and one gastrconemius tendon were treated.

Varying degrees of post injection pain and swelling were noted. Early in the use of this product, 2 horses were non-weight bearing within 24 hours of injection. This led to a modification of aftercare protocol (icing and NSAIDS). Two horses were subsequently significantly painful within 24 hours of injection (for a total of 2.1% of all treated), while 27 horses were mildly to moderately painful (14.2 %). The majority of the treated horses did not demonstrate post injection pain (159 horses or 83.7%). Some mild edema was present in 169 cases 3 days post-injection. The responses of pain and swelling led to establishment of the management protocol mentioned in the previous paragraphs. Medical and physical therapy as previously described dramatically reduced side effects of pain and swelling. Surgical cases demonstrated mild local edema and generally were moderately thickened at the surgical site at thirty days, but all surgical sites were very cosmetic by 90 days with the exception of one that remained thickened with some distal limb edema of unknown origin.

Results of progressive soundness evaluations and client reports of horses 12 months or greater post-treatment were reviewed, and a satisfactory response was judged to be by ability to return to the previous level of work. Results were found as follows: of 77 proximal/body suspensory ligament lesions, 65 were sound and in work and 12 were still convalescing or lame (84.4% recovery); of 15 suspensory branch lesions, 13 were sound and in work and 2 were convalescing or lame (86.7%); of 14 superficial digital flexor tendon lesions, 13 were sound and in work and one was convalescing (92.9%); the one gastrconemius tendon had returned to soundness. A total of 92 of 107 cases or 85.9% of cases that were 12 months or greater post-treatment were sound and in work.

Ultrasound evaluation of post-injection lesions demonstrated significant fluid infiltrate at the 5-day and most 30 day follow-up examinations. In contrast, the 60-day examinations consistently demonstrated good fiber pattern formation and minimal edema in treated lesions. The noted fiber pattern demonstrated good linearity along the lines of stress/loading. Lameness was generally improved at the 60 day post treatment inspection.

Discussion

Equine tendon and ligament injuries are generally regarded as having a predictably prolonged convalescent period with high probability for re-injury. Healing is thought to be prolonged in part due to relatively poor blood supply to the affected tissues and opportunity for re-injury in the daily course of activity. Historically, tendon injuries have often been regarded as taking a full year for recovery often with poor healing quality.⁴ In private practice, topical and internal blisters (coupled with prolonged rest or light exercise) have been the more traditional

means of treating these injuries. Such “counterirritation” may have even been harmful with regard to future athletic function.⁵ In recent years numerous devices have been proposed to be of benefit for tendon and ligament healing, i.e., pulsed magnetic therapy, low-level therapeutic laser, and ultrasound therapy.⁶ Tendon splitting and superior check ligament desmotomy have gained favor for SDF injuries.⁷ Splitting has also gained some acceptance for suspensory body core lesions and suspensory branch lesions. More recently fasciotomy and injection of bone marrow/blood has been suggested to increase the rate and quality of healing in proximal suspensory ligament injuries.⁸ Injection of insulin growth factor (IGF-1) in conjunction with superficial check desmotomy has been promising for SDF injuries in racehorses⁹. Stem cells derived from equine adipose tissue are currently commercially available for tissue repair purposes.

UBM powder is a lyophilized, acellular powder manufactured from the ECM of the urinary bladder of SPF pigs. UBM powder suspension produces a local inflammatory-like response when injected into injured tissue, as evidenced by localized heat, pain, swelling and sometimes mild redness. Histopathology in species other than the equine have indicated a profound angiogenic response developing in the first 5-7 days post treatment in studies where UBM membrane was implanted in tissue. Accompanying this response is the recruitment of bone marrow-derived cells into the treated tissue.^{10 11} As time passes, and tissue heals, implanted UBM membrane is no longer evident histologically and scarring is not present, only normal tissue of the type that was injured.¹² It is proposed that UBM powder containing the same collagen, peptides and other substances of UBM membrane would have a similar effect.

Tendons and ligaments injected with UBM develop profound fiber pattern response by 60 days post injection. Ultrasonographic appearance of these fibers appears very similar to normal tissue. Clinical response and soundness would indicate that affected horses are able to return to moderate activity at an earlier time than with other therapies.

The encouraging results of this investigation suggest the need for a more objective, prospective and blinded investigation of this product for the treatment of ligamentous and tendon injuries in horses. Serial examination of histological samples as healing progresses may help investigators determine the nature of this regenerative process and if UBM is an appropriate therapy for tendon and ligament repair. The commercial availability of products that do not require harvesting and ex vivo expansion would be advantageous to practitioners, potentially safer for the horse, and would allow some flexibility that may not be currently available for treatments that use autogenous mesenchymal stem cells.



Figure 1-SDF Tendon Laceration 3/30/03

Figure 2-SDF Tendon 116 days post UBM

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⁴ Ibid

⁵ Henninger R "Treatment of superficial flexor tendonitis," *Tendon and Ligament Injuries I, Veterinary Clinics of North America, Equine Practice*, 1994, W. B. Saunders; 10-2: 418-419

⁶ Ibid; 414-416

⁷ Ross MW "Surgical management of superficial digital flexor tendonitis," *Diagnosis and Management of Lameness in the Horse*, 2003 W. B. Saunders; 635-639

⁸ Herthel D "Clinical use of stem cells and bone marrow components to stimulate suspensory ligament regeneration," *Diagnosis and Management of Lameness in the Horse*, 2003, W. B. Saunders; 673-674

⁹ Nixon AJ Personal communication, 2004

¹⁰ Badylak S, Obermiller J, Geddes L, Matheny, R "Extracellular matrix for myocardial repair," *The Heart Surgery Forum*, 2003, 6(2) #2002-72222

¹¹ Badylak SF, Park K, Peppas N, McCabe G, Yoder M "Marrow-derived cells populate scaffolds composed of xenogenetic extracellular matrix," *Experimental Hematology*, 2001; 11:1310-18

¹² Badylak SF, Kropp B, McPherson T, Liang H, Snyder PW "Small intestinal submucosa: a rapidly resorbed bioscaffold for augmentation cystoplasty in a dog model," *Tissue Engineering Journal*, 1998 Winter, 4:379-387