

The use of polyacrylamide hydrogels in horses.

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Objectives:

- Understand what polyacrylamide hydrogels are.
- Be updated on what they do in the joint.
- Select good cases to treat.
- Know how polyacrylamide hydrogels “feel” when treating the horse and assure you are in the correct location.

Introduction

Polyacrylamide hydrogels (PAHG) are three-dimensional structures of acrylamide that can be made with variable degrees of cross-linkages resulting in a wide range of physical properties.¹ These hydrogels are inert and biocompatible giving them a large number of applications ranging from gel electrophoresis to tissue augmentation. Polyacrylamide hydrogels have been shown to exhibit low coefficients of friction and have been used for contact lenses and as acellular cartilage implants^{2,3} Viscosupplementation has been an objective of intra-articular therapy for management of osteoarthritis and PAHG can provide a synthetic joint lubrication. The objective of viscosupplementation is to restore the normal lubrication in joints with inflammation and cartilage surface damage.

Polyacrylamide hydrogels are being utilized as a device for intra-articular lubrication in both humans^{4,5} and horses.⁶⁻⁸ This inert material has mechanical properties similar to normal synovial fluid and have recently been shown to effectively decrease friction in both mechanical and interleukin-1 β induced surface damaged cartilage.^{9,10} The polyacrylamide hydrogels have been shown to decrease lameness in horses for prolonged periods of time after treatment administration.

A prospective study of polyacrylamide hydrogel for the treatment of osteoarthritis in 43 horses reported a significant decrease in lameness, 82.5% of the 43 horses were sound at the 2-year follow-up.⁶ In 12 horses with proximal interphalangeal joint osteoarthritis, 8 horses were sound six months after treatment.⁷ Both of these studies utilized a 2.5% polyacrylamide material designed to be a bulking agent. Another polyacrylamide hydrogel being used in humans with osteoarthritis consists of 4% polyacrylamide and this polymer was specifically designed to be minimally reactive in the joint.⁸ In this study of 28 horses that met inclusion criteria, there was a significant ($P < 0.001$) decrease in median lameness score with 23 /28 (82%) of the horses improved based on study criteria.

The PAHGs are discussed interchangeably, however the manufacturers agree that they may not act similarly. A common misunderstanding is that the difference from the 2 commercially available materials is the concentration. Noltrex[®]Vet^a is a 4% PAHG and Arthramid[®] Vet^b is 2.5% PAHG. However, the reason there is a wide range of applications of PAHGs is because they can be very different based on monomer content and percent cross-

linkage.¹¹ There is not a direct comparison available, but published histologic evaluation of synovial membranes from joints treated with the 2 products are dissimilar.^{12,13}

Case Selection

As a newer therapy, initial case selection tended towards chronic osteoarthritic horses refractory to multiple therapies. The general trend was that these horses would improve about 1 lameness grade following treatment and maintain that improvement for 90 to 120 days. As veterinarians became more knowledgeable of the PAHGs, the trend has been towards treating horses earlier in the disease process. Horses that have been treated 1 to 2 times with more traditional hyaluronic acid and corticosteroids may now be treated with PAHG before the osteoarthritis progresses further. Most joints in the horse have been treated with PAHG. Some of the more common applications are noted.

The metacarpal/metatarsal-phalangeal joints in both sport and racehorses may be the most frequently treated joints, likely because of the incidence of pathology. There may be some thickening or filling of the joint notable in the palmar/plantar pouches after treatment that persists 2 to 4 weeks after administration. Repeated administration of Noltrex[®]Vet up to 4 times at 45-day intervals in fetlock joints did not result in any negative effects on cartilage, synovium or biomarkers of cartilage metabolism.^c Distal interphalangeal joints in sport horses may be the next most common application, but the PAHGs have been used in most of the appendicular skeletal joints at this time.

Because of the large size of the stifle joint, some practitioners have used a “double dose” when treating stifles. When utilizing Noltrex[®]Vet, the 2.5 ml dose should be an adequate volume to coat the articular surfaces, so a single dose is likely adequate. On the other end of the scale, tarsometatarsal and distal intertarsal joints are likely well coated with 1 ml. Similarly, when managing bilateral navicular syndrome cases, a syringe may be split between the bursae.

Administration

Because the PAHGs tend to be more viscous than most materials clinicians are used to administering, the “feel” of the material going readily into the joint is different. Larger gauge needles, 18 or 19 ga, are indicated to improve ease of administration. Smaller gauge needles can be used, though the injection should be done slowly and with care to avoid displacing the needle, or disconnecting the needle from the syringe due to pressure. The polyacrylamide will not be eliminated quickly as would a periarticular corticosteroid, so confirmation of intra-articular placement is useful.

PAHGs do not carry an elevated risk for infection following intra-articular injection. The addition of antibiotics can be considered based on the clinician’s preference. Due to their inert and insoluble characteristics, PAHGs are not known to interact with intra-articular antibiotics commonly utilized in the horse, and have been seen combined in some studies.¹⁴ Standard aseptic site preparation, with sterile injection technique, remains the most important method to prevent contamination of the injection site.

Corticosteroids are commonly utilized intra-articular, often in combination with viscosupplements, to control pain and inflammation. There are no known corticosteroid/PAHG combinations that cause interactions between the products. Concurrent administration has been reported by clinicians using PAHG, though no formal investigation has been performed. It is suggested by Arthramid[®] Vet to avoid concurrent corticosteroid administration with their product to prevent down regulating synovial fibroblasts, which encourage cellular proliferation

and vessel ingrowth across the gel incorporated into the synovial membrane. Noltrex[®]Vet is dissimilar in its interaction with the synovial membrane, therefore this mechanism is not relevant when considering its administration with corticosteroids.^{12,13} A double-blinded positive controlled study comparing Arthramid[®] Vet, sodium hyaluronate, and triamcinolone acetonide found that Arthramid[®] Vet treated carpal joints produced significantly more lame-free horses at 4-weeks and 6-weeks post-injection ($P = .042$, $P = .019$, respectively) than hyaluronate or triamcinolone.¹⁵

Horses are rested for 2-3 days, followed by walking exercise for a week, and then low impact exercise with a gradual returning to full exercise over 2-3 weeks. This is a longer period than many therapies, but the response to therapy does not occur rapidly. Response to treatment varies. Some cases show improvement within days after injection, while others may take up to 30 days. Generally, a gradual improvement is seen between 1-3 weeks. If some improvement is noted, but the lameness is not eliminated, the veterinarian should consider a second dose at 5-6 weeks post initial injection.

Limitations

Polyacrylamide is not a quick fix for lameness. They require some rest following therapy and there may be a slow improvement over 2-3 months. Injection technique is important to assure the PAHG is within the synovial cavity.

There have been a few horses that have had an increased lameness for 2-4 weeks following administration. There are two potential causes of this and both may be correct. Periarticular administration can result in swelling and effusion. The PAHG is hydrophilic, resulting in a filling of the joint space. The PAHG in Arthramid[®] Vet was designed as a tissue filler, so it will remain in the subcutaneous tissue an extended period of time. Second, there is the occasional horse that will have an increased lameness and synovitis after work, in the first week or two after treatment. Two plausible explanations for this are impingement of the synovium that may be thicker following administration of the PAHG and pushing of the PAHG into subchondral defects. Overall, knowledge is still limited relative some of the other joint therapies

Conclusions

The understanding of how and when to utilize PAHGs is rapidly evolving. Case selection, injection technique, and post-treatment controlled exercise are important to successfully add these materials to your practice. There are differences in the PAHGs available, so veterinarians need to be familiar with the product they are using and how to best utilize the material.

References and Footnotes

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^a Noltrex[®]Vet, RC Bioform, LLC, Moscow, Russia.

^bArthramid[®] Vet, Contura International A/S, 2860, Søborg, Denmark.

^c McClure SR, Unpublished data, January 2022.