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Archives of Orthopaedics Commentary

# Viscosupplementation in Horses: What do We Really Know?

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The importance of osteoarthritis (OA) is undeniable in equine medicine, with a high occurrence in the routine, several studies have been carried out to understand the pathophysiology of the disease and to seek more efficient methods of prevention and treatment [1,2]. Among the most frequent approaches in the management of this condition, viscosupplementation (VS) with hyaluronic acid (HA) is widely spread and performed [3]. However, there are many doubts about the mechanisms and protocols of treatment using this resource, which calls into question its real benefit [4].

We recently presented a systematic review that discusses the current evidence supporting the use of HA and polyacrylamide hydrogel (PAHG), as intra-articular therapy in horses, and the results found were surprising [4]. Thus, it was concluded at that time, that there was no real evidence of benefits, treatment protocols and mechanisms of action of HA in articular therapy in horses. In addition, none study showing clinical outcome in diseased synovial tissue from PAHG, and was not included because it did not respect the selection criteria.

The conclusions we reached in this article can be impactful for veterinarians who use HA and HGPA in their daily routine, and could immediately challenge these statements. However, a similar position is presented by the American Academy of Orthopaedic Surgeons (AAOS) [5] and the National Institute for Health and Care Excellence (NICE) [6], respected medical institutions internationally, in which they failed to recommend VS in joint therapy, due to the lack of a clinically significant benefit for most patients.

However, we emphasize that this should not lead to the disuse of this type of treatment in OA, but on the other hand, it should encourage the development of studies that seek to understand the real effect of these compounds and under what conditions are indicated. A current and complete review of HA is available and the authors encourage reading as a complement [7].

An objective methodology is an indispensable tool to reduce bias in scientific works. In our review, most articles were excluded for using lameness scores at different times of assessment, based on subjective assessment, that is, visual inspection. This has already been proven to be inherent in bias, even among experienced evaluators [8]. It does not seem to us, the most appropriate, to use this type of methodology to base the considerations on the outcomes. The evolution of the clinical signs is a crucial point in the interpretation of the effectiveness of the treatment of any condition.

Regardless of the findings of the imaging examination, the reduction or abolition of lameness, and how long this situation remains, is the most critical factor for the absolute satisfaction of the owner. This makes us reflect on the importance of an objective assessment of lameness, so that bias-free considerations are made.

It is important to highlight that an MRI evaluation is generally used to construct the diagnosis in human patients, which leaves no doubt about what is happening in the affected joint. In horses it do not occur, in most cases only radiographic and ultrasound exams are available to characterize the condition, methods that have their limitations and depend largely on the examiner's skill and experience [9,10].

The financial factor has great influence, usually a single application is made and the products with lower costs are used. The products with cheaper formulations have a lower degree of purity and less noble origin, this increases the risk of joint flare. What can trigger an acute inflammatory response, for a short period - a few days - putting its potential effect at risk, and can even get worse the joint [11]. Johnston et al. [12] evaluated

the effects of two HA formulations intra-articular with different molecular weights and analyzed the parameters of lameness, joint effusion and synovial fluid in healthy horse joints. In this study, joints injected with HA formulations demonstrated significant mild to moderate inflammatory responses, often associated with lameness and joint effusion, compared to the control group.

Improving methods bring important advances and can change how to understand. In this sense, Cook and Bonassar [13], tested the traditional rheological measurements of HA and observed that the current methodology may not adequately measure this variable. The metallic accessories of the equipment do not capture the effect of the localization of HA, which occurs in the cartilage. Thus, they investigated the effect of modifying rheometric devices with cartilage surface coatings on the effective viscosity of HA solutions. They demonstrated a 20-fold increase in effective viscosity when HA was confined between cartilage surfaces compared to metal surfaces. For low molecular weight HA, the effective viscosity depended on the height of the space between the rheometer plates, which is consistent with the formation of a viscous contour film. Together, these results indicate that this method for assessing the viscosity of HA may be more relevant for lubrication than traditional methods and may provide a more accurate method for predicting the viscosity of HA viscosupplements *in vivo*.

Campos et al. [14] presented the 'Brazilian Consensus on Viscosupplementation', which through a multidisciplinary panel reached a consensus on several aspects of VS, for example: the best indication is for mild to moderate knee arthrosis; previous or concomitant use of intra-articular triamcinolone hexacetonide can optimize the effect of HA; VS should not be performed as an isolated procedure in the treatment of OA, but in conjunction with other rehabilitation and pharmacological measures; promotes analgesic effect; anti-inflammatory; chondroprotective. These considerations may be reasonable to be extrapolated to horses, but they lack scientific confirmation.

In relation to PAHG, since the publication of our article, the new studies available still support its positive outcomes in subjective assessments of lameness [15]. In relation to human studies, synthetic polyacrylamide hydrogels have been used in the treatment of knee OA, but adverse events are documented, such as inflammation, joint pain and joint effusion, which limit clinical use [16,17].

Since OA is a multifactorial disease, a treatment that is efficient must be multimodal. Therefore, the combination of drugs and therapies, physical therapy, adjustment of physical activities must be formulated for each case, preceded by an accurate diagnosis. The VS is an important tool and has potential application among the various presentations. As discussed by Rezende and Campos [18], we do not know if there is a better product, but we do know that there are products with different characteristics. We believe that the knowledge on the part of professionals about the HA that they will use is important, taking into account its characteristics.

## References

1. Schlueter AE, Orth MW. Equine osteoarthritis: a brief review of the disease and its causes. Equine and Comparative Exercise Physiology. 2004 Nov;1(4):221-31.

2. McIlwraith CW. Principles and practices of joint disease treatment. In: Diagnosis and Management of Lameness in the Horse 2011 Jan 1 (pp. 840-852). WB Saunders.

3. Goodrich LR, Nixon AJ. Medical treatment of osteoarthritis in the horse–a review. The Veterinary Journal. 2006 Jan 1;171(1):51-69.

4. Souza AF, Paretsis NF, Zoppa ALV. What is the evidence of hyaluronic acid and polyacrylamide hydrogel in intra-articular therapy in equines? Systematic literature review. Journal of Equine Veterinary Science. 2020 Jan 7;86:102909.

5. American Academy of Orthopaedic Surgeons (AAOS). Treatment of Osteoarthritis of the Knee: Evidence-Based Guideline. 2nd ed. Rosemont, IL: AAOS; 2013 [Available from: https://www.aaos.org/globalassets/quality-and-practice-resources/osteoarthritis-of-the-knee/osteoarthritis-of-the-knee-2nd-editiion-clinical-practice-guideline.pdf]. Accessed April 28, 2020.

6. Conaghan P, Birrel F, Porcheret M, Doherty M, Dziedzic K, Bernstein I, et al. Osteoarthritis: care and management in adults. clinical guideline 177. National Clinical Guideline Centre. 2014;1–498. https://www.nice.org.uk/guidance/cg177/evidence/full-guideline-pdf-191761311. Accessed April 27, 2020.

7. Gupta RC, Lall R, Srivastava A, Sinha A. Hyaluronic acid: Molecular mechanisms and therapeutic trajectory. Frontiers in Veterinary Science. 2019;6:192.

8. McCracken MJ, Kramer J, Keegan KG, Lopes M, Wilson DA, Reed SK, LaCarrubba A, Rasch M. Comparison of an inertial sensor system of lameness quantification with subjective lameness evaluation. Equine Veterinary Journal. 2012 Nov;44(6):652-6.

9. Biggi M, Dyson S. Comparison between radiological and magnetic resonance imaging lesions in the distal border of the navicular bone with particular reference to distal border fragments and osseous cyst-like lesions. Equine Veterinary Journal. 2010 Nov;42(8):707-12.

10. Olive J, D'Anjou MA, Alexander K, Laverty S, Theoret C. Comparison of magnetic resonance imaging,

computed tomography, and radiography for assessment of noncartilaginous changes in equine metacarpophalangeal osteoarthritis. Veterinary Radiology & Ultrasound. 2010 May;51(3):267-79.

11. Kuemmerle JM, Uhlig H, Kofler J. Severe acute inflammatory reaction (SAIR) of the fetlock joint after intraarticular hyaluronate injection in a horse. Veterinary and Comparative Orthopaedics and Traumatology. 2006;19(04):236-8.

12. Johnston GC, Wood KA, Jackson KV, Perkins NR, Zedler ST. Evaluation of the inflammatory response to two intra-articular hyaluronic acid formulations in normal equine joints. Journal of Veterinary Pharmacology and Therapeutics. 2020 Jan;43(1):38-49.

13. Cook SG, Bonassar LJ. Interaction with Cartilage Increases the Viscosity of Hyaluronic Acid Solutions. ACS Biomaterials Science & Engineering. 2020 Apr 13;6(5):2787-95.

14. Campos GC, Sousa EB, Hamdan PC, Júnior A, Tieppo AM, Rezende MU, Alchaar AA, Pinheiro CB, Rocha ED, Cunha FG, Pacheco I. Brazilian consensus statement on viscosupplementation of the knee (cobravi). Acta Ortopédica Brasileira. 2019 Aug;27(4):230-6.

15. de Clifford LT, Lowe JN, McKellar CD, Bolwell C, David F. Use of a 2.5% Cross-Linked Polyacrylamide Hydrogel in the Management of Joint Lameness in a Population of Flat Racing Thoroughbreds: A Pilot Study. Journal of Equine Veterinary Science. 2019 Jun 1;77:57-62.

16. Tonbul M, Adas M, Bekmezci T, Kara AD. Intra-articular polyacrylamide hydrogel injections are not innocent. Case Reports in Orthopedics. 2014;2014:150709.

17. Mandal A, Clegg JR, Anselmo AC, Mitragotri S. Hydrogels in the clinic. Bioengineering & Translational Medicine. 2020 May; 5(2): e10158.

18. Uchôa de Rezende M, Constantino de Campos G. Viscosupplementation. Revista Brasileira de Ortopedia. 2012;47(2):160-164.