

The role of viscosupplementation injection in treatment of osteoarthritis and soft tissue injuries

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Abstract: Hyaluronic acid viscosupplementation is one of most popular options in nonsurgical management of osteoarthritis. Recent clinical studies have proved that the anti-inflammatory, anabolic, and chondroprotective actions of hyaluronic acid reduce pain and improve patient function. Viscosupplementation with hyaluronic acid is safe and effective in the management of osteoarthritis, but its use in the treatment of other soft tissue pathologies such as tendonopathy, subacromial bursitis, and partial rotator cuff tears has received less attention. This article describes physiological functions, basic pharmacological properties, and the clinical use of hyaluronic acid. Also reviews the use of intra-articular hyaluronic acid viscosupplementation in the management of knee osteoarthritis and presents the potential for expanding its indications for other joints. Additionally, summarizes the current knowledge on using viscosupplementation in management of different soft tissue disorders, evaluating experimental and clinical trials in this topic.

[Younis Mahmoud Akl, Emad Mohammed Zayed and Ahmed Magdy Ahmed Arafa. **The role of viscosupplementation injection in treatment of osteoarthritis and soft tissue injuries.** *N Y Sci J* 2017;10(1):10-12]. ISSN 1554-0200 (print); ISSN 2375-723X (online). <http://www.sciencepub.net/newyork>. 2. doi:[10.7537/marsnys100117.02](https://doi.org/10.7537/marsnys100117.02).

Keywords: knee; hyaluronic acid; osteoarthritis; viscosupplementation; tendonopathy

Introduction

Viscosupplementation is the name that was given to the use of hyaluronan solutions, alone or in combination with gel particles, used to replace and supplement the pathological synovial fluid (**Balazs, 2009**).

Hyaluronic acid (hyaluronan, HA) is a linear polysaccharide formed from disaccharide units containing N-acetyl-D-glucosamine and glucuronic acid. It has a high molecular mass, usually in the order of millions of Daltons, and interesting viscoelastic properties influenced by its polymeric and polyelectrolyte characteristics (**Grigorij et al., 2007**).

The biological functions of HA include maintenance of the elastoviscosity of liquid connective tissues such as joint synovial and eye vitreous fluid, control of tissue hydration and water transport, supramolecular assembly of proteoglycans in the extracellular matrix, and numerous receptor-mediated roles in cell detachment, mitosis, migration, tumor development and metastasis, and inflammation (**Balazs and Denlinger, 1989**).

Its function in the body is, amongst other things, to bind water and to lubricate movable parts of the body, such as joints and muscles. Its consistency and tissue-friendliness allows it to be used in skin-care products as an excellent moisturizer. Hyaluronic acid is one of the most hydrophilic (water-loving) molecules in nature and can be described as nature's moisturizer (**Necas, et al., 2007**).

The unique viscoelastic nature of HA along with its biocompatibility and non-immunogenicity has led to its use in a number of clinical applications, including the supplementation of joint fluid in arthritis, as a surgical aid in eye surgery, and to facilitate the healing and regeneration of surgical wounds (**Barbucci, et al., 2002**).

Hyaluronic acid (HA) is an important component of articular cartilage; it is present as a coat around chondrocytes, where it bounds to aggrecan monomers, which imbibe water and are responsible for the resilience of cartilage (i.e., resistance to compression) (**Abate, et al., 2010**).

Several clinical trials have shown that viscosupplementation therapy with HA is safe and effective in the management of osteoarthritis (OA) resistant to conventional therapies (**Rutjes, et al., 2012**).

Despite the positive results in OA, its use in the treatment of tendon disorders has received less attention. Actually, HA is actively secreted by the tendon sheath and, as for joints, it is an important component of the synovial fluid, which allows a smooth tendon gliding, and provides nutrition to tendon itself (**Hagberg, et al., 1992**).

Moreover, it is an important component of tendon structure, being largely present in extracellular space (**Abate, et al., 2014**).

Use of Hyaluronic acid in Different osteoarthritis

Hyaluronic acid (HA), also known as hyaluronan or hyaluronate, is a high-molecular-weight glycosaminoglycan composed of continuously repeating molecular sequences of glucuronic acid and N-acetyl-glucosamine (**Brockmeier and Shaffer, 2006**).

In addition to providing joint lubrication and shock absorbancy, HA acts as the backbone for the proteoglycans of the extracellular matrix, creating a hydrated pathway through which cells can migrate (**Hempfling, 2007**).

Recent studies have also suggested that HA promotes chondrocyte proliferation and differentiation, which has spurred interest in its use as a scaffold component in tissue-engineering techniques (**Yagishita et al., 2005**).

In the arthritic joint, the concentration and molecular weight of HA are decreased by 33% to 50%, limiting its role in maintaining normal joint biomechanics (**Smedsrod, 1991**).

The purpose of viscosupplementation is to replace the lost HA and potentially stimulate the production of endogenous HA within the joint (**Bagga, et al., 2006**).

Although at the present time the exact mechanism of action is not completely understood, recent research suggests that HA exerts anti-inflammatory, analgesic, and possibly chondroprotective effects on the articular cartilage and joint synovium (**Strauss, et al., 2009**).

Hyaluronic acid preparations differ with respect to origin, method of production, treatment schedule, molecular weight, half-life within the synovium, rheologic properties, pharmacodynamics, and cost (**Altman, et al., 2006**).

Although intra-articular HA injection is currently indicated and FDA approved for treating pain associated with OA of the knee, recent studies demonstrating beneficial results with respect to pain reduction and functional improvement have led to increased off-label use for OA of the hip, shoulder, and ankle (**Altman, et al., 2005**).

The Use of Hyaluronic acid in soft tissue injuries and different Tendinopathies

HA has been mostly used after a surgical procedure for tendon injuries or in the treatment of chronic tendinopathies (**Abate, et al., 2014**).

HA is an essential component of the tendon itself. It is well known that, after experimental damage, tendon healing process proceeds along a complex pathway beginning with inflammation and cellular proliferation and followed by tissue formation and maturation, with each phase lasting for days, weeks, and months, respectively (**Andia, et al., 2010**).

Briefly, in the damaged area, the injury molecular products stimulate an acute inflammatory reaction with the secretion of cytokines, reactive

oxygen species, cationic peptides, or proteases (**Abate, et al., 2014**).

This phase is followed by cell proliferation, collagen and matrix deposition, and tissue remodeling and the final outcome is scar tissue formation, which can partially restore tendon function. Indeed, the mechanical properties are compromised for years, due to composition of the extracellular matrix and its organization (**Abate, et al., 2014**).

Basic research has shown that the activity of hyaluronidase is increased in granulation tissue during the healing of equine superficial digital flexor tendon injuries, suggesting that HA plays a relevant role in controlling the healing process in equine tendonitis (**Foland et al., 1992**).

Experimental research and pivotal clinical trials suggest that HA is effective in preventing adhesions after flexor tendons surgery. Different preparations and procedures are at present under study to define the best option (**Abate, et al., 2014**).

Promising results have been also observed in the treatment of tendinopathies. In general terms, the positive effect relies on the anti-inflammatory activity of HA, enhanced cell proliferation, and collagen deposition, besides the lubricating action on the sliding surface of the tendon (**Abate, et al., 2014**).

However, it must be underlined that in the majority of studies the drug was not injected inside the degenerated tendon, but nearby and/or into the articular space. It can be speculated that the modifications of the synovial fluid can exert a positive effect on the tendon itself, but it cannot be excluded that the clinical improvement may be secondary to the positive action on osteoarthritis frequently associated (**Abate, et al., 2014**).

Conclusion

Intra-articular HA injection is gaining popularity as part of the nonoperative management of patients with OA. The anti-inflammatory, anabolic, and chondroprotective actions of HA have been shown in recent clinical studies to reduce pain and improve function.

With evidence mounting in support of the efficacy of this treatment modality for patients with OA, its potential use in additional patient populations and other pathologies affecting the knee is being investigated. Although continued study is needed, intra-articular HA injection is proving to be a safe, effective, and evolving tool for clinicians treating patients with symptomatic OA.

There has been recent interest in the use of HA for treatment of soft tissue pathology such as tendinopathy, subacromial bursitis, and partial rotator cuff tears particularly in younger athletic population. The proposed mechanism of action of HA in the soft

tissues is poorly understood, but there is in vitro evidence that HA reduces the rate of degeneration of tendon matrix components and stimulate proteoglycan synthesis.

References

1. Abate M., Schiavone C., Salini V., The use of hyaluronic acid after tendon surgery and in tendinopathies.2014, Biomed Res Int 2014;783632.
2. Abate M., Pulcini D., Di Iorio A., and Schiavone C. "Viscosupplementation with intra-articular hyaluronic acid for treatment of osteoarthritis in the elderly," Current Pharmaceutical Design, 2010, vol. 16, no. 6, pp. 631–640.
3. Altman RD, Cohen MM, Hollstrom R, Efficacy of intra-articular hyaluronan (Hyalgan) in a double-blind study for osteoarthritis of the ankle. *Osteoarthritis Cartilage*. 2006;14(suppl B): S170.
4. Altman RD, Moskowitz R, Jacobs S, Double-blind, randomized trial of intra-articular injection of sodium hyaluronate (Hyalgan) for treatment of chronic shoulder pain. *Arthritis Rheum*. 2005;52 (suppl): S461.
5. Andia I., Sanchez M., and Maffulli N., "Tendon healing and platelet-rich plasma therapies," Expert Opinion on Biological Therapy,2010, vol. 10, no. 10, pp. 1415–1426.
6. Bagga H, Burkhardt D, Sambrook P, March L., Longterm effects of intraarticular hyaluronan on synovial fluid in osteoarthritis of the knee. *J Rheumatol*. 2006;33(5):946-950.
7. Balazs E.A., Denlinger J.L., Clinical uses of hyaluronan. *Ciba Found Symposium*,1989, 143, 265–275.
8. Balazs EA., Therapeutic use of hyaluronan, *Struct Chem*, 2009 (20):341–349.
9. Barbucci R., Lamponi S., Borzacchiello A., Ambrosio L., Fini M., Torricelli P., Giardino R., Hyaluronic acid hydrogel in the treatment of osteoarthritis. *Biomaterials*,2002, 23, 4503–4513.
10. Brockmeier SF., Shaffer BS., Viscosupplementation therapy for osteoarthritis. *Sports Med Arthrosc*. 2006;14(3):155-162.
11. Eric J. Strauss, Jennifer A. Hart, Mark D. Miller, Roy D. Altman and Jeffrey E. Rosen, Hyaluronic Acid Viscosupplementation and Osteoarthritis: Current Uses and Future Directions, *Am J Sports Med* 2009, 37: 1636-1644.
12. Foland J.W., Trotter G.E., Powers B.E., Wrigley R.H., and Smith F.W., "Effect of sodiumhyaluronate in collagenase-induced superficial digital flexor tendinitis in horses," *American Journal of Veterinary Research*,1992, vol. 53, no. 12, pp. 2371–2376.
13. Grigorij K., Ladislav S., Robert S., Peter G.. Hyaluronic acid: a natural biopolymer with a broad range of biomedical and industrial applications. *Biotechnol Letts*. 2007 (29):17–25.
14. Hagberg L., Heinegard D., and Ohlsson K., "The contents of macromolecule solutes in flexor tendon sheath fluid and their relation to synovial fluid; A quantitative analysis," *Journal of Hand Surgery*,1992, vol. 17, no. 2, pp. 167–171.
15. Hempfling H., Intra-articular hyaluronic acid after knee arthroscopy: a two-year study. *Knee Surg Sports Traumatol Arthrosc*. 2007;15(5): 537-546.
16. Necas J., Bartosikova L., Brauner P., Kolar J., Hyaluronic acid (hyaluronan): a review, *Veterinari Medicina*, 53, 2008 (8): 397–411.
17. Rutjes A.W., Juni P., Costa B.R., Trelle S., Nuesch E., and Reichenbach S., "Viscosupplementation for osteoarthritis of the knee: a systematic review andmeta-analysis," *Annals of Internal Medicine*,2012, vol. 157, no. 3, pp. 180–191.
18. Smedsrod B., Cellular events in the uptake and degradation of hyaluronan. *Advanced Drug Delivery Reviews*, 1991, 7, 265–278.
19. Yagishita K., Sekiya I., Sakaguchi Y., Shinomiya K., Muneta T., The effect of hyaluronan on tendon healing in rabbits. *Arthroscopy*. 2005;21(11): 1330-1336.

12/24/2016