

Viscosupplementation for Glenohumeral Arthritis



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Abstract

Visupupmentation for the treatment of glenohumeral arthritis is a non-surgical treatment capable of improving joint mobility and relieving symptoms. Its intra-articular administration has been shown to be beneficial for synovial liquid properties, protective and reparative for the joint structure. However, there are currently few studies with good methodology and clinical results. The objective of this study was to conduct a review of the literature on the viscosupplementation of hyaluronic acid in glenohumeral arthritis to evidence and clarify the published results on the improvement of pain, function, range of motion and improvement period. Orthopedic medical literature was reviewed in the Medline, Pubmed, Regional Medicine Library (BIREME) and Cochrane Libery databases.

Keywords: Viscosupplementation; Viscosupplementation shoulder; Glenoumeral Arthritis; Viscosupplementation Glenoumeral arthritis; Arthritis Shoulder

Introduction

Glenohumeral arthritis is characterized by gradual, progressive, mechanical degeneration of the cartilage and joint capsule, synovial membrane and subchondral bone. Pathology very common in the elderly, and according to the American College of Rheumatology, almost 60% of people over 70 years present radiographic evidence of glenohumeral arthritis [1-3]. The evolution of this pathology establishes the loss of joint mobility and is one of the main reasons for persistent pain in the shoulder [2]. Despite its increased incidence, the range for clinical treatment remains limited. In early cases of glenohumeral arthritis, analgesic medications, physiotherapy, infiltrations with corticosteroids and hyaluronic acid (viscosupplementation) are usually chosen [4,5].

Visupupmentation is non-surgical treatment capable of improving joint mobility and relieving symptoms. Its intra-articular administration has been shown to be beneficial for the properties of the synovial fluid, which is protective and reparative for the joint structure [6]. The largest of these studies, Blaine et al. [7] studied 660 patients and concluded that hyaluronic acid was effective and safe in the treatment of cases with glenohumeral arthrosis, with or without the accompaniment of pathologies of the shoulder.

Hyaluronic Acid

Hyaluronic acid (HA) has been used in medical practice for over fifty years. Under normal conditions, it is the main constituent of extracellular matrix and synovial fluid. It presents properties for joint lubrication, cartilage protection, joint pressure distribution and mechanical shock absorption [5]. Provides nutrition and transmits cellular signals to articular cartilage [3]. It is a high molecular weight glycosaminoglycan, a high viscosity polysaccharide produced in B cells. It provides viscoelasticity and protects cartilage and adjacent tissues [8]. It is a structure of 3 to 30 μm , with non-sulfated and unbranched glycosaminoglycan as the main structure attached to a disaccharide N-acetyl glucosamine and glucuronic acid [9].

AH decreases the cytokine gene expression, thus there is a lower production of prostaglandins and a decrease in metalloproteases (MMPs), responsible for the degradation of cartilage. The viscosupplementation stimulates the creation of endogenous hyaluronic acid, has analgesic effects, reduces nerve impulses and sensitivity in the nociceptive endings, elevates the chondrocyte multiplication, promotes the production of collagen type 2 and aggrecanos and reduces the degradation of type 2

collagen [10]. Stimulates metabolism and inhibits chondrocyte apoptosis, chondral degradation and inflammatory responses [11].

In osteoarthritis, the concentration of HA is reduced, the effects of dilution, reduction of synthesis of hyaluronan and degradation of free radicals are mainly responsible. Thus the transmission of mechanical force to the articular cartilage can facilitate its susceptibility to mechanical damages [12]. The objective of this study is to perform an update with a review of the literature on the viscosupplementation of hyaluronic acid in glenohumeral arthritis to update, to highlight the already published results on the improvement of pain, function, range of motion and the period of improvement.

Materials and Methods

A review of the orthopedic medical literature was carried out in the Medline, Pubmed, Cochrane Libery and Regional Medicine Library (BIREME) database, with the following combinations: viscosupplementation glenohumeral arthritis, hyaluronic acid glenohumeral arthritis, hyaluronic acid, high molecular weight, viscosupplementation shoulder in english. The studies were selected directing them to the subject of intra-articular injection of hyaluronic acid in patients with glenohumeral arthritis and clinical evolution being described in english. All studies (prospective, retrospective, review, technique for infiltration) were analyzed. There was no time boundary of the publication. All studies, after study of the methodology, that did not conduct the viscosupplementation in patients with glenohumeral arthritis were excluded.

After applying the search criteria, 24 studies were selected.

Infiltration Technique

Hyaluronic acid loses its effectiveness when administered extra-articularly and can cause pain and formation of granulomas at the site of its administration. El attrache et al have obtained cadaveric studies, 80% of correct injection intra-articular by the anterior approach without imaging aid, and only 50% with posterior approach [13]. Values consistent with the Tobola et al study, in which 65% of correct injection intra-articular by the anterior approach, 46% were posterior approach and 46% were those for the supraclavicular approach [14]. However Esenyel et al. [15] found by the anterior approach, analysis of 50 shoulders in cadavers, an accuracy of 96%. The repositioning of the needle was free as needed, and viscosupplementation performed by an experienced orthopaedist.

When ultrasonography and radioscopy are not used, the technical error rates reach 40 to 80% [16,17]. Patel et al compared the accuracy of guided palpation versus ultrasonography for viscosupplementation. Ultrasonography was performed in 73% of patients with palpation and 93% of ultrasonography [18]. Rutten et al. [19] analyzed 100 patients, ultrasound versus radioscopy, anterior and posterior approach. All cases in both groups were intra-articular and confirmed by

magnetic resonance imaging; however, ultrasonography showed a higher percentage of hits in the first attempt (94% versus 72% radioscopy).

Hyaluronic Acid X Corticoid

In a recent systematic review study with 32 papers, the efficacy of AH was demonstrated in 8 studies, however the vast majority of studies were of low level of evidence with failed methodology. Although the difference in efficacy between placebo and AH was small, the improvement in patients with viscosupplementation during the first 6 months was significant (grade A of recommendation). The corticoid treatment, also analyzed in the systematic review, is reported only in a single retrospective case-control study, showing very low efficacy (grade B of recommendation) and the fact that the risks of the use are serious, it is concluded that there are recommendations for the use of intra-articular corticoid injections for patients with glenohumeral arthritis¹.

Merolla et al. [20] in a retrospective analysis studied patients with glenohumeral arthritis submitted to Hylan G-F 20 joint infiltration (62 patients) compared to 6-methylprednisolone (41 cases). The groups were correlated with the severity of glenohumeral arthritis with clinical outcomes (pain, function, Constant-Murley score). Better results were observed with viscosupplementation for pain and function. The efficacy of steroid injection with good results was only for pain in the first month after treatment. Patients affected by mild to moderate glenohumeral OA achieved significant reduction and pain satisfaction for up to 6 months after treatment with intra-articular HA injections. Cases with advanced osteoarthritis presented worse scores and evolved to arthroplasties.

Hyaluronic Acid of High Molecular Weight

Intra-articular injection can be performed with hyaluronic acid of different molecular weights. Porcellini and col performed viscosupplementation in 41 patients with high molecular hyaluronic acid. The improvement of pain, function and bow of movement with 3 months of evolution was visualized. However, there was no control group and the follow-up was short-term [3]. Di Giacomo G et al. [21] applied high molecular weight injections in patients with moderate and severe glenohumeral osteoarthritis. Three intra-articular injections with HA (Hyalubrix, 30 mg / 2 mL, molecular weight > 1,500 kDa) associated with rehabilitation versus the sole physiotherapy treatment. In 78 patients in the study, it was found that cases affected by moderate to severe OA that received intra-articular injection treatment in association with physical therapy had a better outcome in terms of pain reduction. There was no evidence of a difference in WMD between the two different types of treatment. In addition, pain reduction achieved an improvement in glenohumeral function and daily life activity [2,3].

Noel E. et al. [22] showed that in 29 patients, with no other associated pathologies (rotator cuff rupture, adhesive

capsulitis) submitted to high molecular weight hyaluronic acid (Hylan GF 20) at 3 months, the visual analogue scale decreased significantly from 61,2 to 37,1. About 52% of the cases presented improvement after the first intra-articular application, which lasted up to 6 months.

Hyaluronic Acid X Clinical Results

Di Giacomo et al. [21] Evaluated the clinical and functional effect of glialoumeral arthritis (I, II, III) after intrarticular viscosupplementation (HA (Hyalgan 20mg / 2ml) combined with physical therapy, 31 patients, versus only physiotherapy, 30 patients. (p <0.05), both of which showed significant improvement in both external elevation and rotation (p <0.05) In contrast to the study by Merolla et al, all grades of glenohumeral arthritis achieved better results for ADM, daily activity and pain22. Silverstein et al. Reported the outcome of 30 cases, with significant improvement of pain, function, without side effects, up to 6 months after intra-articular application (Hylan G-F 20) in 3 doses. No addition of cases to the study of pathology of the rotator cuff [23].

Valiveti et al. [23] found mild to moderate improvement for pain and mobility in 11 patients for 4 months of follow-up, but all cases were moderate or severe osteoarthritis [24]. In a multicenter, randomized, double-blind, controlled study the efficacy and safety of the application of intra-articular HA (molecular weight, 500 to 730KDa) for pain and functional limitation with glenohumeral arthritis, adhesive capsulitis and rupture of the rotator cuff. It was applied in 660 patients. There was improvement of the analog pain scale in patients with glenohumeral arthritis at 7 to 26 weeks with 3 to 5 applications and better results compared to cases in which patients did not present glenohumeral arthritis. However, the improvement in pain was not constant throughout the follow-up and after 32 weeks the follow-up was completed [7].

Conclusion

Intra-articular injections of hyaluronic acid for mild and moderate osteoarthritis have proved to be a valid alternative for conservative treatment. Improvement of function, daily activities and pain relief up to 6 months after application of the drug was shown. In cases of severe osteoarthritis there was no significant clinical improvement. For the articular infiltration, the anterior portal guided by ultrasonography or fluoroscopy showed better accuracy rates compared to posterior and supraclavicular. The viscosupplementation AH for osteoarthritis is a promising therapeutic option but lacks prospective trials to better assess its long-term efficacy and safety.

References

1. Colen S, Geervliet P, Haverkamp D, Van Den Bekerom MP (2014) Intra-articular infiltration therapy for patients with glenohumeral osteoarthritis: a systematic review of the literature. *Int J Shoulder Surg* 8(04): 114–121.
2. Di Giacomo G, de Gasperis N (2017) Hyaluronic Acid Intra-Articular Injections in Patients Affected by Moderate to Severe Glenohumeral Osteoarthritis: A Prospective Randomized Study. *Joints* 5(3): 138-142.

3. Balazs EA, Denlinger JL (1993) Viscosupplementation: a new concept in the treatment of osteoarthritis. *J Rheumatol Suppl* 39: 3–9.
4. Porcellini G, Merolla G, Giordan N, Paladini P, Burini A, et al. (2016) Intra-articular glenohumeral injections of HYADD@4-G for the treatment of painful shoulder osteoarthritis: a prospective multicenter, open-label trial. *Joints* 3(03): 116–121.
5. Kwon YW, Eisenberg G, Zuckerman JD (2013) Sodium hyaluronate for the treatment of chronic shoulder pain associated with glenohumeral osteoarthritis: a multicenter, randomized, double-blind, placebo-controlled trial. *J Shoulder Elbow Surg* 22(05): 584–594.
6. Abatangelo G, o'Regan M (1995) Hyaluronan: biological role and function in articular joints. *Eur J Rheumatol inflamm* 15: 9-16.
7. Blaine T, Moskowitz R, Udell J, Skyhar M, Levin R, et al. (2008) Treatment of persistent shoulder pain with sodium hyaluro-nate: a randomized, controlled trial. A multicenter study. *J Bone Joint Surg Am* 90(5): 970-979.
8. Gigis I, Fotiadis E, Nenopoulos A, Tsitas K, Hatzokos I (2016) Comparison of two different molecular weight intra-articular injections of hyaluronic acid for the treatment of knee osteoarthritis. *Hippokratia* 20(1): 26-31.
9. Fransson L (1985) Mammalian glycosaminoglycans. In: ASPINALL, G. (Ed.) *The Polysaccharides*. Academic Press, Inc. St Louis, Missouri, USA, p. 51-337.
10. Gomis A, Pawlak M, Balazs EA, Schmidt RF, Belmonte C, et al. (2004) Effects of different molecular weight elastoviscous hyaluronan solutions on articular nociceptive afferents. *Arthritis Rheum* v 50(1): 314-326.
11. Schiavinato A, Finesso M, Cortivo R, Abatangelo G (2002) Comparison of the effects of intra-articular injections of Hyaluronan and its chemically cross-linked derivative. *Clin Exp Rheumatol* 20(4): 445-454.
12. Abate M, Pulcini D, Di Iorio A, Schiavone C (2010) Viscosupplementation with intra-articular hyaluronic acid for treatment of osteoarthritis in the elderly. *Curr Pharm Des* 16(6): 631–640.
13. Sethi PM, El Attrache N (2006) Accuracy of intra-articular injection of the glenohumeral joint: a cadaveric study. *Orthopedics* 29: 149-152.
14. Tobola A, Cook C, Cassas KJ, Hawkins RJ, Wienke JR, et al. (2011) Accuracy of glenohumeral joint injections: comparing approach and experience of provider. *J. Shoulder Elbow Surg* 20: 1147-1154.
15. Esenyel CZ, Ozturk K, Demirhan M, Mesut Sonmez, Sinan Kahraman, et al. (2010) Accuracy of anterior gleno- humeral injections: a cadaver study. *Arch. Orthop. Trauma Surg* 130(3): 297Y300.
16. Conrozier T (2016) Optimizing the effectiveness of viscosupplementation in non-knee osteoarthritis. *Joint Bone Spine* 83(1): 1-2.
17. Hall MM (2013) The accuracy and efficacy of palpation versus image-guided periph- eral injections in sports medicine. *Curr Sports Med Rep* 12(5): 296–303.
18. Patel DN, Nayyar S, Hasan S, , Khatib O, Sidash S, et al. (2012) Comparison of ultrasound-guided versus blind glenohumeral injections: a cadaveric study. *J. Shoulder Elbow Surg* 21: 1664Y8.
19. Rutten MJ, Collins JM, Maresch BJ, Smeets JH, Janssen CM, et al. (2009) Glenohumeral joint injection: a comparative study of ultrasound and fluoroscopically guided techniques before MR arthrography. *Eur Radiol* 19: 722-730.
20. Merolla G, Sperling JW, Paladini P, Porcellini G (2011) Efficacy of Hylan G-F 20 versus 6-methylprednisolone acetate in painful shoulder osteoarthritis: a retrospective controlled trial. *Musculoskelet Surg* 95(03): 215–224.

21. Di Giacomo G, De Gasperis N (2015) The role of hyaluronic acid in patients affected by glenohumeral osteoarthritis. *J Biol Regul Homeost Agents* 29(04): 945–951.
22. Noël E, Hardy P, Hagena FW, Laprelle E, Goebel F, et al. (2009) Efficacy and safety of Hylan G-F 20 in shoulder osteoarthritis with an intact rotator cuff. Open-label prospective multicenter study. *P Joint Bone Spine* 76(6): 670–673.
23. Valiveti M, Reginato AJ, Falasca GF (2006) Viscosupplementation for degenerative joint disease of shoulder and ankle. *J Clin Rheumatol* 12(3): 162-163.
24. Silverstein E, Leger R, Shea KP (2007) The use of intra-articular hylan G-F 20 in the treatment of symptomatic osteoarthritis of the shoulder: a preliminary study. *Am J Sports Med* 35(06): 979–985.



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