

THE EFFECT OF HYALURONIC ACID IN TREATMENT OF TEMPOROMANDIBULAR JOINT DISORDERS

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ABSTRACT:

There are many different techniques and methods that have been used to treat temporomandibular joint disorders. Intra-articular injections of hyaluronic acid (HA) is one of these methods. The purpose of this article was to review the literature on role of hyaluronic acid injection in the treatment of temporomandibular joint disorders and its effectiveness in improving the pain and functional problems.

Key Words: Hyaluronic acid, Intra-articular injections, Temporomandibular joint disorder, degenerative disorder.



INTRODUCTION

In recent years the medical uses of hyaluronic acid (HA) have been diversified, to include several therapeutic and cosmetic fields.^[1-3,7,9,13]

Hyaluronic acid has been used in intra-articular injection for treatment of various disorders of the joints, including osteoporosis. Previous studies had shown therapeutic efficacy of this procedure^[4-6]. The treatment of TMJ disorders is one of the targets of intra-articular HA injection.^[7-10]

This paper reviews the scientific articles that talk about hyaluronic acid in the treatment of TMJ disorders.

HYALURONIC ACID (HA):

Hyaluronic acid (HA) is a natural polysaccharide belonging to the family of glycosaminoglycans and can be found in many extracellular tissues including SF

and cartilage, This material contributes to ease the function of articular cartilages and make it more effective, this is due to its special properties similar to synovial fluid including the viscosity, lubricating and damping which can be noted in cases like shock absorption and load distribution.^[11] HA is produced by chondrocytes and synoviocytes in the joints.

HA has mechanical, biological and metabolic functions. The first property is lubrication and reduction of wearing out of articular elements.

The biological property: studies in vitro and in vivo demonstrated significant action of HA in blocking of different inflammatory mediators such as TNF- α , IL-1 β , IL-17, PGE2 and induces nitric oxide synthase (iNOS), as well as inhibiting expression of enzymes that

degrade the extracellular matrix such as matrix metalloproteinases (MMPs) 1, 3, 2, 9 and 13. Also HA provides the necessary components of the metabolic process for the articular disc and cartilage. [6,12-16]

TEMPOROMANDIBULAR JOINT DISORDERS (TMD):

Temporomandibular joint disorder (TMD) is a widely researched disease in the literature, since it has a high prevalence and is often associated with chronic pain and limited function of the temporomandibular joint (TMJ), resulting in decreased quality of life for the patient. [17-21]

TMD affect the jaw joints and related structures and includes painful myofacial problems, internal derangement of joint space, abnormalities of bony components, and degenerative and rheumatologic problems. TMD is characterized by pain, joint noise, a limited range of motion, impaired jaw function, deviation or deflection upon mouth opening, malocclusion, and closed or open locking. [18,22]

The etiology is thought to be multifactorial. The capsular inflammation or damage and muscle pain or spasm may be caused solely or in combination by abnormal occlusion, para-functional habits, stress, anxiety, or abnormalities of the intra-articular disk. There is some evidence suggesting that anxiety, stress, and other emotional disturbances may exacerbate TMJ

disorders, especially in those patients who experience chronic pain. [23]

The joint disorders include disc displacement and degenerative and/or inflammatory disorders. Due to its complex etiology and varied classification, different conservative and surgical treatments have been studied in an attempt to improve clinical symptoms and restore function for the affected patients. [17,24-28]

HYALURONIC ACID IN TMJ DISORDERS:

TMJ disorder related to pain in the joint or surrounding tissues and functional limitations associated or not with joint sounds during movement. [18]

Magnetic resonance imaging (MRI) is the most commonly used method for TMJ's soft tissue examination, computed tomography (CT) is for the imaging diagnosis of TMJ alterations which related to bone tissues. [40]

Many nonoperative approaches have been proposed through the years, including occlusal splint therapy, physiotherapy, pharmacotherapy, and arthrocentesis. [29-32]

Many materials have been used in intra-articular injection therapy include non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, botulinum toxin, blood, platelet rich plasma (PRP) and hyaluronic acid. [9,17,26,33-39]

Using CT Images, Møystad et al. compared bone changes after HA and corticosteroid injections to treat TMJ osteoarthritis^[40], They used contralateral TMJ with minor symptoms as the control, and radiographic signs of the disease were classified through a score (presence of erosions, sclerosis, osteophytes, and flattening of the condyle). After 6 months, there was no statistically significant difference between the groups or between the period before and 6 months after treatment. However, progression, regression, and no changes of osteoarthritic abnormalities were observed on CT examinations in both the treated and the contralateral TMJs after treatment with intra-articular injection with sodium hyaluronate or corticosteroid.

The aim of Hegab et al. study^[38] was to compare the use of Platelet-Rich Plasma Injection (PRP) and hyaluronic acid (HA) in the treatment of TMJ osteoarthritis (OA), PRP performed better than HA in the treatment of TMJ-OA during long-term follow-up in terms of pain reduction and increased interincisal distance. Patients received 3 injections of 1 mL of PRP in group II, patients received 3 injections of 1 mL of low-molecular-weight HA. The outcome variables were maximum nonassisted mouth opening (MVMO), joint sounds, and pain index scores. Between-group comparisons of the outcome variables over time revealed significant improvements in group II at 1 and 3 months. At 6 and 12 months, the PRP

group exhibited better performance compared with the HA group in terms of the recurrence of pain and joint sounds. The improvements obtained with the PRP injections in group I were maintained during the follow-up period.

In 2014 Gencer et al.^[18] compared the effect of intra-articular injections of Hyaluronic acid, corticosteroid (betamethasone), and NSAID (tenoxicam) on the relief of temporomandibular joint disorder complaints and they evaluated with CT to investigate the presence of cartilage or capsule degeneration. The patients were randomly divided into four groups consisting of a control group of patients who received saline injections, and the evaluation of pain relief was performed after 1 and 6 weeks. They found that HA produced better pain relief scores (at 1 and 6 weeks) when compared to the other groups and all of them had greater pain relief than the control group. pain relief was not maintained between these periods.

Alpaslan et al.^[27], Kopp et al.^[28,37] reported that TMJ pain symptoms had been improved by intra-articular injections of corticosteroids, but adverse local effects can occur in the joint tissues. Kopp et al. showed that both procedures reduced the clinical symptoms and dysfunction.^[28] On other hand, the more suitable treatment and less risk of the progression of joint degeneration was with HA injections because it is a physiological component of synovial fluid.

Kopp et al.^[37], Bjørnland et al.^[25] compared between HA and corticosteroid injections in treatment of TMJ osteoarthritis, but with a shorter follow-up period. The evaluation time was at 14th day, 1 month, and 6 months, the HA injections group showed a greater pain relief and improvement in jaw function than the second group (corticosteroid injections). The joint sounds improved in both groups. But they reported that temporary pain occurred with HA injections.

Arthrocentesis can be combined with or without hyaluronic acid injections.^[41-43] According to the authors combination treatments gained superior results.^[27,33,44-46] Alpaslan et al. showed that the HA reducing the actions of inflammatory mediators and increasing joint mobility, provides a long-term lubricating effect, .^[27] Whereas, Aktas et al. suggested that arthrocentesis that associated with HA is necessary when there is degeneration of the joint.^[41]

In contrast Emes et al. investigated the effect of NSAID injections in comparison with arthrocentesis associated with HA injections.^[17] Findings showed that the pain decreased between periods in HA injections group while the pain reduced in the first week, but increased after 1 and 3 months of follow-up. The difference was not statistically significant in both groups. The authors show that there is little benefit in using relatively conservative methods once an arthrocentesis together with viscosupplementation has failed to

relieve the patients pain. It is concluded that more invasive procedures (repeated injections, arthroscopy, and surgery) should be considered for the patients who do not benefit from arthrocentesis.

Through several studies Guarda-Nardini et al. suggested a protocol (five arthrocentesis sessions associated with viscosupplementation with HA)^[9,20,34,42,47,48] and they reported improvement in symptoms and TMJ's functions. A similar protocol was followed by Sato S, Oguri et al. in 2001]36 [and in 2006 to treat non-reducing disc displacement]49[. In 2012 Guarda-Nardini et al. compared the effectiveness of 2 treatment protocols 5-session single-needle arthrocentesis plus low- or medium-molecular weight Ha, Similar positive effectiveness was shown for 2 treatment protocols for TMJ osteoarthritis]50[. Again in 2015 Guarda-Nardini et al. compared the effectiveness of two single-session protocols, either adopting high- (protocol A) or medium-molecular weight hyaluronic acid (protocol B), with the reference five-session protocol of temporomandibular joint (TMJ) lavage plus viscosupplementation (protocol C) in the management of chronic TMJ degenerative disorders, The five-session protocol was significantly superior to both single-session protocols.^[51]

The aim of Manfredini et al. study was to compare six treatment protocols, (Arthrocentesis with or without additional drugs in TMJ inflammatory-degenerative)^[52], Randomly assigned to

one of the groups: single-session two-needle arthrocentesis (A), single-session two-needle arthrocentesis plus corticosteroid (B), single-session two-needle arthrocentesis plus low molecular weight hyaluronic acid (HA) (C), single-session two-needle arthrocentesis plus high molecular weight HA (D), 5 weekly two-needle arthrocenteses plus low molecular weight HA (E) and 5 weekly single-needle arthrocenteses plus low molecular weight HA (F). At the 3-month follow-up, The protocol number (C) allowed achieving the highest improvement in almost all the outcome variables (chewing efficiency, pain at rest and in motion, and improvement in mouth opening values), no statistically significant differences existed between the treatment groups. Also Guardia-Nardini et al.^[48] investigation did not support the existence of significant differences in the treatment effectiveness for inflammatory-degenerative TMJ disorders of a cycle of five weekly injections of arthrocentesis plus hyaluronic acid injections performed according to the classical two-needle or the single-needle technique.

Kopp et al.^[53] compared the effects of HA, glucocorticoids, and saline solution injections to treat TMJs Rheumatoid arthritis (RA), A comprehensive clinical dysfunction values were reduced significantly in all groups, while the number of tender muscle regions was significantly reduced and the maximum voluntary mouth opening significantly increased in the

glucocorticoid and sodium hyaluronate groups only.

CONCLUSION:

Intra-articular injections of hyaluronic acid (HA) is a beneficial method in the treatment of temporomandibular joint disorders, There is no specific protocol to be followed in the procedures of injections. However, other drug such as corticosteroid and NSAID injections can be used with good results.

REFERENCES:

1. Rzany B et al. Full-face rejuvenation using a range of hyaluronic acid fillers: efficacy, safety, and patients satisfaction over 6 months. *Dermatol Surg* 2012;38(7 Pt 2):1153–61.
2. Colen S et al. Hyaluronic acid in the treatment of knee osteoarthritis: a systematic review and meta-analysis with emphasis on the efficacy of different products. *BioDrugs* 2012,26(4):257–268.
3. Juni P et al. Efficacy and safety of intraarticular hylan or hyaluronic acids for osteoarthritis of the knee: a randomized controlled trial. *Arthritis and rheumatism*. 2007; 56(11):3610–9.
4. Tang T et al. Serum keratan sulfate transiently increases in the early stage of osteoarthritis during strenuous running of rats: protective effect of intraarticular hyaluronan injection. *Arthritis Res Ther* 2008;10(1):R13.
5. Huang GS et al. Quantitative MR T2 measurement of articular cartilage to assess the treatment effect of intra-

- articular hyaluronic acid injection on experimental osteoarthritis induced by ACLX. *Osteoarthr Cartil* 2010;18(1):54–60.
6. Campo GM et al. Hyaluronan reduces inflammation in experimental arthritis by modulating TLR-2 and TLR-4 cartilage expression. *Biochim Biophys Acta* 2011;1812(9):1170–81.
 7. Hegguler S et al. The efficacy of intra-articular sodium hyaluronate in patients with reducing displaced disc of the temporomandibular joint. *J Oral Rehabil* 2002;29:80-6.
 8. Guarda-Nardini L et al. Conservative treatment of temporomandibular joint osteoarthrosis: intra-articular injection of sodium hyaluronate. *J Oral Rehabil* 2005;32:729-34.
 9. Guarda-Nardini L et al. A one-year case series of arthrocentesis with hyaluronic acid injections for temporomandibular joint osteoarthritis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;103: e14-22.
 10. Yeung RWK et al. Short-term therapeutic outcome of intra-articular high molecular weight hyaluronic acid injection for nonreducing disc displacement of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;102:453-61.
 11. De Leeuw R. *Dor orofacial: guia de avaliac, ão. In: diagnóstico e tratamento. 4th. São Paulo: Quintessence; 2010.*
 12. Neo H et al. The effect of hyaluronic acid on experimental temporomandibular joint osteoarthrosis in the sheep. *J Oral Maxillofac Surg* 1997;55(10):1114–9.
 13. Wang CT et al. High molecular weight hyaluronic acid down-regulates the gene expression of osteoarthritis-associated cytokines and enzymes in fibroblastlike synoviocytes from patients with early osteoarthritis. *Osteoarthr Cartil* 2006;14(12):1237–47.
 14. Hsieh YS et al. Effects of different molecular weight hyaluronan products on the expression of urokinase plasminogen activator and inhibitor and gelatinases during the early stage of osteoarthritis. *J Orthop Res* 2008;26(4):475–84.
 15. Hashizume M et al. High molecular weight hyaluronic acid relieved joint pain and prevented the progression of cartilage degeneration in a rabbit osteoarthritis model after onset of arthritis. *Mod Rheumatol* 2010;20(5):432–8.
 16. Shimizu M et al. Clinical and biochemical characteristics after intra-articular injection for the treatment of osteoarthritis of the knee: prospective randomized study of sodium hyaluronate and corticosteroid. *J Orthop Sci* 2010;15(1):51–6.
 17. Emes Yet al. The next step in the treatment of persistent temporomandibular joint pain following arthrocentesis: a retrospective study of 18 cases. *J Craniomaxillofac Surg* 2014;42:e65–9.
 18. Gencer ZK et al. A comparative study on the impact of intra-articular injections of hyaluronic acid, tenoxicam and betametazon on the relief of temporomandibular joint disorder complaints. *J Craniomaxillofac Surg* 2014;42:1117–21.
 19. Su N, Yang X et al. Evaluation of arthrocentesis with hyaluronic acid injection plus oral glucosamine hydrochloride for temporomandibular joint osteoarthritis in oral-health-

- related quality of life. J Craniomaxillofac Surg 2014;42:846–51.
20. Guarda-Nardini L et al. Predictive factors of hyaluronic acid injections short-term effectiveness for TMJ degenerative joint disease. J Oral Rehabil 2011;38:315–20
21. Tang YL et al. Effects of intra-articular administration of sodium hyaluronate on plasminogen activator system in temporomandibular joints with osteoarthritis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109:541–7.
22. Leeuw R: Temporomandibular disorders. In: Leeuw R (ed.), American academy of orofacial pain guidelines for assessment, diagnosis and management, 4th edn. Chicago: Quintessence, 131e133,2008
23. Okeson JP, for the American Academy of Orofacial Pain: *Orofacial pain: guidelines for assessment, diagnosis, and management. Chicago, Ill: Quintessence Pub. 1996*
24. Manfredini D et al. psychosocial findings predict effectiveness of TMJ hyaluronic acid injections. Int J Oral Maxillofac Surg 2013;42:364–8.
25. Bjørnland T et al. Osteoarthritis of the temporomandibular joint: an evaluation of the effects and complications of corticosteroid injection compared with injection with sodium hyaluronate. J Oral Rehabil 2007;34:583–9.
26. Babadag M et al. Pre-and posttreatment analysis of clinical symptoms of patients with temporomandibular disorders. Quintessence Int 2004;35:811–4
27. Alpaslan GH, Alpaslan C. Efficacy of temporomandibular joint arthrocentesis with and without injection of sodium hyaluronate in treatment of internal derangements. J Oral Maxillofac Surg 2001;59:613–8.
28. Kopp S et al. The short-term effect of intra-articular injections of sodium hyaluronate and corticosteroid on temporomandibular joint pain and dysfunction. J Oral Maxillofac Surg 1985;43:429–35
29. Turp JC et al. Efficacy of stabilization splints for the management of patients with masticatory muscle pain: A qualitative systematic review. Clin Oral Investig 8:179, 2004
30. Nicolakis P et al. Effectiveness of exercise therapy in patients with myofascial pain dysfunction syndrome. J Oral Rehabil 29:362, 2002
31. Dionne RA: Pharmacologic treatments for temporomandibular disorders. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 83:134, 1997
32. Yura S et al. Can arthrocentesis release intracapsular adhesions? Arthroscopic findings before and after irrigation under sufficient hydraulic pressure. J Oral Maxillofac Surg 61:1253, 2003
33. Morey-Mas MA, et al. Sodium hyaluronate improves outcomes after arthroscopic lysis and lavage in patients with Wilkes stage III and IV disease. J Oral Maxillofac Surg 2010;68:1069–74.
34. Manfredini D et al. Temporomandibular joint osteoarthritis: an open label trial of 76 patients treated with arthrocentesis plus hyaluronic acid injections. Int J Oral Maxillofac Surg 2009;38:827–34.
35. Oliveras-Moreno JM et al. Efficacy and safety of sodium hyaluronate in the treatment of Wilkes stage II disease. J Oral Maxillofac Surg 2008;66:2243–6

36. Sato S et al. Pumping injection of sodium hyaluronate for patients with non-reducing disc displacement of the temporomandibular joint: two year follow-up. *J Craniomaxillofac Surg* 2001;29:89–93
37. Kopp S et al. Long-term effect of intra-articular injections of sodium hyaluronate and corticosteroid on temporomandibular joint arthritis. *J Oral Maxillofac Surg* 1987;45:929–35
38. Ayman F. Hegab et al. Platelet-Rich Plasma Injection as an Effective Treatment for Temporomandibular Joint Osteoarthritis. *J Oral Maxillofac Surg*:1-8, 2015
39. Ayman F. Hegab. Treatment of chronic recurrent dislocation of the temporomandibular joint with injection of autologous blood alone, intermaxillary fixation alone, or both together: a prospective, randomised, controlled clinical trial. *British Journal of Oral and Maxillofacial Surgery* 51 (2013) 813–817
40. Møystad A et al. Injection of sodium hyaluronate compared to a corticosteroid in the treatment of patients with temporomandibular joint osteoarthritis: a CT evaluation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008;105:e53–60.
41. Aktas I et al. Prognostic indicators of the outcome of arthrocentesis with and without sodium hyaluronate injection for the treatment of disc displacement without reduction: a magnetic resonance imaging study. *Int J Oral Maxillofac Surg* 2010;39:1080–5.
42. Guarda-Nardini L et al. Short-term effects of arthrocentesis plus viscosupplementation in the management of signs and symptoms of painful TMJ disc displacement with reduction. A pilot study. *Oral Maxillofac Surg* 2010;14:29–34.
43. Triantafyllidou K et al. Efficacy of hyaluronic acid injections in patients with osteoarthritis of the temporomandibular joint. A comparative study. *J Craniofac Surg* 2013;24:2006–9.
44. Alpaslan C et al. D. Effect of arthrocentesis and sodium hyaluronate injection on nitrite, nitrate, and thiobarbituric acid-reactive substance levels in the synovial fluid. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;89:686–90.
45. Tuncel U. Repeated sodium hyaluronate injections following multiple arthrocenteses in the treatment of early stage reducing disc displacement of the temporomandibular joint: a preliminary report. *J Craniomaxillofac Surg* 2012;40:685–9.
46. Bertolami CN et al. Use of sodium hyaluronate in treating temporomandibular joint disorders: a randomized, double-blind, placebo-controlled clinical trial. *J Oral Maxillofac Surg* 1993;51:232–42.
47. Guarda-Nardini L et al. Intra-articular injection of hyaluronic acid for temporomandibular joint osteoarthritis in elderly patients. *Stomatologija* 2009;11:60–5.
48. Guarda-Nardini L et al. Two-needle vs. single-needle technique for TMJ arthrocentesis plus hyaluronic acid injections: a comparative trial over a sixmonth follow up. *Int J Oral Maxillofac Surg* 2012;41:506–13.
49. Sato S, Kawamura H. Changes in condylar mobility and radiographic alterations after treatment in patients with non-reducing disc displacement of the

- temporomandibular joint.
Dentomaxillofac Radiol 2006;35:289–94.
50. Luca Guarda-Nardini, et al. Comparison of 2 Hyaluronic Acid Drugs for the Treatment of Temporomandibular Joint Osteoarthritis. *J Oral Maxillofac Surg* 2012;70:2522-2530.
51. Guarda-Nardini L et al. Single or multiple-session viscosupplementation protocols for temporomandibular joint degenerative disorders: a randomized clinical trial. *J Oral Rehabil* 2015;42:521–8.
52. Manfredini D et al. Arthrocentesis with or without additional drugs in temporomandibular joint inflammatory-degenerative disease: comparison of six treatment protocols. *J Oral Rehabil* 2012;39:245–51.
53. Kopp S et al Short-term effects of intra-articular sodium hyaluronate, glucocorticoid, and saline injections on rheumatoid arthritis of the temporomandibular joint. *J Craniomandib Disord* 1991;5:231–8.