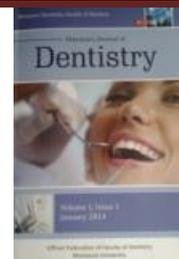




## *Intra articular injection of collagen versus hyaluronic acid for treatment of pain and joint noise in anterior disc displacement of the temporomandibular joint.*



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### **Abstract:**

**Background:** Anterior disc displacement with reduction (ADDWR) is one of the most common temporomandibular disorders (TMDs). Many medications have been used for intra-articular injection in TMJ for treatment of ADDWR. One of the widely used medications is Hyaluronic acid (HA) due to its biological functions inside body joints. Collagen also has a very crucial role for keeping integrity of joints which has never been intra-articularly injected for treatment of any TMD.

**Aim of the study:** The aim of this study is to compare the intra-articular injection of collagen versus HA as a treatment of Anterior disc displacement of TMJ.

**Methodology:** 29 patients (30 joints) seeking treatment of ADDWR were randomly divided into two groups, group I patients were injected with collagen, while group II were injected with HA. The two groups were evaluated at 1 week, 1 month and 3 months post-operatively to the second injection according to Modified Helkimo's index for TMDs and according to lateral range of motion (lateral movement).

**Results:** No significant difference was found between the two groups in any of the evaluation variables.

**Conclusion:** the result confirms the crucial roles of HA as beneficial medication for treatment of ID and other TMDs. Also, it gives the chance for further investigations of collagen as a treatment of TMDs.

**Keywords:** Internal Derangement, Collagen, Hyaluronic acid, Intra-articular injection

### **Introduction**

TMDs are generally classified into extra- and intra-articular types. Intra-articular disorders include internal derangement, osteoarthritis and inflammatory arthritis and muscular, vascular, and neurologic diseases of extra-articular origin. The TMJ's internal derangement (ID) means that there is an altered condyle-disc-fossa relationship that interfere with the joint's smooth function. It accounts for 25% of TMJ disorders.

Various interventions have been proposed for management of A.D.D.W.R. Nonsurgical, including physical therapy, drug therapy, splint therapy, arthrocentesis, intra-articular injection etc., and invasive surgical intervention which includes disc repair and repositioning, discectomy condylotomy, arthroscopy, etc. Many agents have been proposed as an intra-articular injection material for treatment of anterior disc displacement with reduction including corticosteroids, hyaluronic acid (HA), non-steroidal anti-inflammatory drugs (NSAIDs), dextrose, blood concentrates like platelet rich fibrin (PRF) and platelet rich plasma (PRP), ozone gas and even botulinum toxin type A (Botox).

Hyaluronic acid (HA) is considered one of the most effective agents that's commonly used in intra-articular injection for treatment of ID signs and symptoms. Its action comes from its several biological functions in joint space such as lubrication, scavenging free radicals, regulating cellular activity and filling joint spaces. In addition to its unusual rheological properties which enable HA to be injected through small pore needle

Collagen represents the quarter of mammalian protein mass. It plays a very crucial role in dealing with the loads

on the joint's structures (discs, muscles, tendons and ligaments). This is due to Anisotropy which is considered one of the most prominent properties of collagen. Lately in various studies <sup>(9)</sup>, it has been intra-articularly injected in knees and couple of small joints for treatment of clinical signs and symptoms of osteoarthritis and myofascial pain. However, up to our knowledge, there is no previous study evaluated the effect of collagen intra-articular injection on any temporomandibular disorder.

### **Methodology:**

29 patients (30 joints; 28 females and 1 male) seeking treatment of symptoms of anterior disk displacement were selected from the Outpatient Clinic of Oral and Maxillofacial Surgery department, Faculty of Dentistry, Mansoura University. They were diagnosed with ADDWR through clinical signs and symptoms. The age ranged from 18-50 years with mean age 31 years.

The patients were randomly divided into 2 groups; group I patients were injected with collagen (Guna collagen MD-small joints)\*through 2 injections over 2 weeks (1ml / week). Group II patients were injected with HA (Gengigel syringe)\*\*through 2 injections over 2 weeks (0.5 ml / week). The clinical manifestations were recorded according to Modified Helkimo's index for TMDs regarding Pain with movement (P), joint noise (S). Each variable has a

\* (Guna collagen MD-small joints)®: GUNA S.P.A, Via Palmanova 71, 20132 Milano, Italy.

\*\*Gengigel® 0.8% PROF.: Ricefarma, Milano, Italy.

score from 0-5 according to the severity of the manifestations. Before the procedure, every patient was informed about the procedures, the aim of the study, and the possible complications. A signed informed consent was obtained from each of patients.

After scrubbing the skin overlying the TMJ with 10% Povidone-iodine solution and plugging the external auditory meatus with a cotton pledge, auriculotemporal nerve was anesthetized. The superior joint space was localized 10 mm anterior to the tragus and 2 mm below the canthal tragus line (Fig.1). For group I, 1 ml of collagen preparation was drawn from a ready-made vial (Guna collagen MD-small joints) in a plastic disposable 3 cc 29g syringe. For group II, 0.5 ml of HA (Gengigel syringe) comes in a ready-made syringe, so a 29 g needle was mounted to the syringe hub. The needle then is slowly inserted to the point of injection into the SJS and the amount of the medication is slowly injected (Fig. 1). After that, the needle was slowly withdrawn and the patient was asked to gently manipulate his mandible in protrusive, vertical and lateral excursions to free up the disc.

The patients were given Instructions for soft diet and home physical therapy (moist heat and mandibular exercises 4 times daily for 1 month) and Antibiotic: Amoxicillin + clavulanic acid\* 625 mg tablet three times daily for prophylaxis of any joint space infection (three times a day) for 5 days. Ibuprofen\*\* 600mg tablets also was prescribed three times daily as an anti-inflammatory as it needed.

Patients were evaluated at 1 week, 1 month and 3 months from the time of the second injection, for improvement of signs and symptoms according to modified Helkimo's index for evaluation of temporomandibular dysfunction<sup>(13)</sup> regarding Pain (P), joint noise (S). at 1 week, 1 month and 3 months from the time of the second injection. Finally, the collected data were analyzed to compare between the two groups.

## Results:

**Regarding pain (P) in group I**, there was a significant improvement among all intervals ( $P = 0.00$ ) when pre-operative pain was compared to that of 1 week ( $P = 0.001$ ), 1 month ( $P = 0.005$ ) and three months after the second injection. In group II, there was a significant difference between all intervals in group II ( $P=0.00$ ) when preoperative pain was compared pain at 1 week ( $P = 0.001$ ), 1 month ( $P= 0.001$ ) and three months ( $P= 0.001$ ) from the second injection. Also, there is a significant difference in the improvement of pain at 1 month compared to 1 week ( $P= 0.014$ ) and 3 months compared to 1 week ( $P= 0.02$ ). When group I and group II were compared for improvement of pain there was no significant difference ( $P > 0.05$ ) in the degree of pain at any of three post-operative follow up intervals 1 week ( $P= 0.88$ ), 1 month ( $P= 0.21$ ) and 3 months ( $P = 0.06$ ).

**Regarding joint noise in group I**, there was a significant difference among all the intervals ( $P = 0.00$ ) when pre-operative noise compared to that after 1 week ( $P = 0.00$ ), 1 month ( $P = 0.00$ ), and three months ( $P = 0.00$ ), from the second injection. In group II, there was a significant difference among all the intervals ( $P= 0.00$ ) when pre-operative noise was compared to that after 1 week ( $P = 0.00$ ), 1 month ( $P$  value = 0.00) and 3 months ( $P= 0.00$ ) from the second injection. When the 2 groups were compared to each other no significant difference was found at 1 week ( $P$  value = 0.30), 1 month ( $P$  value = 0.33) and three months ( $P$  value = 0.33).

## Discussion:

Several medications have been injected intra-articularly for treatment of several TMDs such as HA, corticosteroids, NSAIDs, IPRF, PRP and dextrose. This study compared the intra articular injection of collagen versus that of HA for treatment of anterior disc displacement with reduction. Up to our knowledge, this is the first study to include intra articular injection of collagen for treatment of any of TMDs. The previous studies that used collagen were in other joints such as knees, ankles and wrists.

Regarding pain (P) at Group I, patients showed a significant improvement which may coincide with Friedrichs J et al.<sup>(14)</sup>, Del Nogal et al.<sup>(15)</sup>, and Hynes<sup>(16)</sup> who described the anisotropy of collagen fibers and its crucial role in force distribution and transmission to the fibroblasts which forms collagen itself and help in tissue repair. This study also come in accordance with V. Reshkova et al.<sup>(10)</sup> who reported significant improvement in joint movements without pain after intra-articular injection of collagen in patients with knee osteoarthritis. Milani L. et al.<sup>(11, 12)</sup> also mentioned that promising results were recorded after intra-articular injection of collagen in 10 clinical trials including small joints.

**For group (II), the reduction of pain (P)**, coincides with what was mentioned by Alpaslan and Alpaslan<sup>(17)</sup>; Kopp et al.<sup>(18)</sup> and Bjørnland et al.<sup>(19)</sup> who compared intra-articular injection of HA versus that of corticosteroids and reported superior results in HA groups. The results also coincide with Tamer TM<sup>(7)</sup> and Yamaguchi et al.<sup>(20)</sup> who mentioned that HA act as a free radical's scavenger which in turn reduces the hyperalgesia and joint pain produced from these radicals. On the other hand, another studies conducted by Kopp et al.<sup>(21)</sup> showed no significant difference between HA and corticosteroid groups who showed no improvement in signs and symptoms of other TMDs which is in contrary to the results of the current study. The disagreement may be attributed to the difference in the severity of signs and symptoms of osteoarthritis and internal derangement.

**Considering joint noise (S) in group I**, the results are parallel to the theory of Stegenga BJJ<sup>(26, 27)</sup>, Dijkgraaf LC et al.<sup>(28)</sup> who hypothesized that disc displacement can be a result of overloading the articular surfaces beyond their limits and damage and fibrillation of collagen fibers that results in increasing friction and adhesion ending by loss of

\*Augmentin 625 mg @:GlaxoSmithKline Malta Limited, Registered in Malta No C38750. Registered Office: 1, First Floor, De La Cruz Avenue Qormi, QRM2458, Malta.

\*\*BRUFEN® 600 mg tablets: Abbott Egypt, Cairo, Egypt

co-ordination of the condylar disc complex during mandibular movements and joint noise. Also, the hydro-dissection caused by the injection may explain the reduction of joint noise in group I patients.<sup>(29,30)</sup>

In group II, **reduction of joint noise (S)** can be attributed to the role of HA in lubrication keeping smooth co-ordinate movement subsequently absence of joint noise which coincides with the studies of Nitzan D<sup>(31, 32)</sup>, Zardeneta et al.<sup>(33)</sup>, and Tomida et al.<sup>(34)</sup>.

Group II results also coincides with Schumacher et al.<sup>(35)</sup> and who reported that HA is responsible for holding and trapping Proteoglycan 4 (PRG4) AKA (lubricin) between the articular surface providing an important lubrication mechanism and less friction and stickiness which leads to joint noise.

The limitations of the current study are Small sample size in both groups, lack of knowledge of the appropriate

dose and number of collagen injection due to absence of any previous use of collagen in for treatment of any temporomandibular disorder, difficulty of obtaining the collagen vials and relative high cost of both HA and collagen.

#### Conclusion:

Despite the limitation of our study especially the lack of previous studies on intra-articular collagen injection in TMJ, the results of our studies open the door for further investigations on intra-articular injection of collagen in TMJ and if it can be used with other types of ID or any TMD. On the other hand, the results confirm HA as a beneficial material to be used for treatment of signs and symptoms of TMDs.

**Table 7: Mann-Whitney Test and its statistical significance in comparing pain (P) in different intervals for group I and group II based on Modified Helkimo's Index for temporomandibular dysfunction:**

Intervals	Mean Rank		Z Value	P value
	Group I	Group II		
Pre-operative (P)	14.50	14.50	0.00	1.00
1 week (P)	14.29	14.71	-0.15	0.88
1 month (P)	16.21	12.79	-1.27	0.21
3 months (P)	17.21	11.79	-1.89	0.06

**Table 17: Mann-Whitney Test and its statistical significance in comparing Signs of TMJ noise and disc derangement (S) in different intervals for group I and group II, based on Modified Helkimo's Index for temporomandibular dysfunction:**

Intervals	Mean Rank		Z Value	P value
	Group I	Group II		
Pre-operative	13.79	15.21	-0.52	0.61
1 week	15.93	13.07	-1.04	0.30
1 month	15.71	13.29	-0.98	0.33
3 months	15.71	13.29	-0.98	0.33



(Fig.1): a clinical intra-operative photograph showing A: localization of the anatomical land mark and the needle insertion point (black arrow); B: a clinical intra-operative photograph showing the injection of collagen in one of group I patients.

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