



*M.I.A.M. Sakr, A.Y. Eman,  
M.S.A. Wael*

## SUMMARY

– **Introduction** – Internal mechanical imbalance is one of the most frequent Temporomandibular Disorders (TMDs), and various drugs injected intra-articularly into the Temporomandibular Joint (TMJ) have been used to treat it.

Collagen, an essential molecule for maintaining joint integrity, has never been injected intra-articularly for the treatment of any TMD.

– **Objective of the study** – To evaluate the effects of intra-articular injection of collagen in pain related to internal TMJ imbalance.

– **Materials and Methods** – 20 patients (20 joints) undergoing treatment for internal TMJ imbalance were injected with 2 ml of MD-SMALL JOINTS (1 ml per week).

The patients were evaluated at 1 week, 1 month, and 3 months after the second injection according to the pain parameter of the modified Helkimo's Index for TMDs.

– **Results** – A statistically significant improvement of pain was found in all follow-up intervals.

– **Conclusions** – The results confirm the fundamental role of collagen in preserving the integrity of all joints. Furthermore, these results open the doors to further research on collagen as a treatment for TMDs.

## KEY WORDS

TMJ, INTERNAL MECHANICAL IMBALANCE, COLLAGEN, INTRA-ARTICULAR INJECTION, MEDICAL DEVICE, MD-SMALL JOINTS

# EVALUATION OF PAIN RELATED TO INTERNAL MECHANICAL IMBALANCE OF THE TEMPORO-MANDIBULAR JOINT AFTER INTRA-ARTICULAR INJECTION OF MD-SMALL JOINTS

## INTRODUCTION

Temporo-mandibular Disorders (TMDs) are nosologically classified into extra- and intra-articular types.

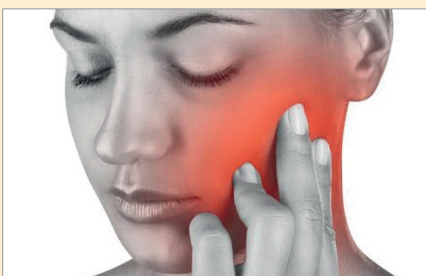
– The internal imbalance of the Temporomandibular Joint (TMJ) implies an altered condyle-disc-fossa connection so to interfere with the joint smooth function.

It accounts for 25% of all TMJ disorders (Hall *et Al.*, 1984; Daif, 2012).

– To treat the internal imbalance of the TMJ, different solutions have been pro-

posed, both nonsurgical, including Physiotherapy, pharmacological therapy, functional devices, arthrocentesis, intra-articular injections – and surgical options, such as disc repair and repositioning, discectomy, condylotomy, etc. (Slater & de Leeuw, 2019).

Some substances have been proposed as an intra-articular injection material for the treatment of anterior disc displacement with reduction; these include corticosteroids, hyaluronic acid (HA), non-steroidal anti-inflammatory drugs (NSAIDs), dextrose, blood concentrates like Platelet Rich Fibrin (PRF) and Platelet Rich Plasma (PRP), ozone



<https://www.towsonmddentist.com/dental-services/restorative-dentistry/tmj-treatment/>

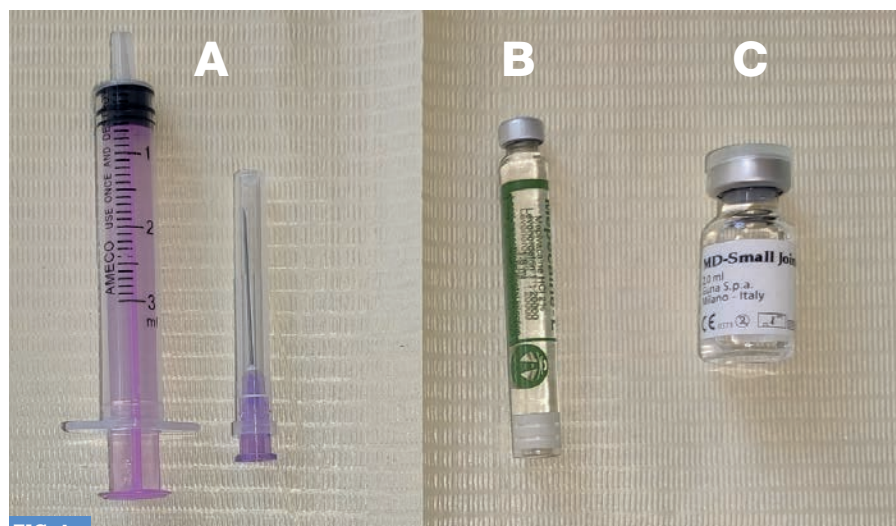


FIG. 1

**Materials used in the study.**

- A - Plastic disposable syringe (3 cc) with 25-gauge needle.**
- B - Mepivacaine HCl 2% with Levonordefrin 1:20,000.**
- C - MD-SMALL JOINTS.**

gas, and botulinum toxin type A (Botox) (Daif, 2012; Gencer *et al.*, 2014; Fernández-Ferro *et al.*, 2017; Bahgat *et al.*, 2018; Slater & de Leeuw, 2019).

– Collagen represents a quarter of total protein mass in Mammalians. This protein plays a crucial role in dealing with the loads on the joint structures

(discs, capsules, ligaments, muscles, tendons) thanks to anisotropy, which is considered one of its most prominent properties.

Lately in various studies (e.g., Reshkova *et al.*, 2016), collagen has been injected intra-articularly in knees and in some small joints for the treatment of clinical signs and symptoms of osteoarthritis and myofascial pain (Alfieri, 2016).

As far as we know, up to now no clinical studies evaluating the effects of collagen intra-articular injections in temporomandibular disorders have been published (Milani, 2013; 2019; Alfieri; 2016).

**MATERIALS AND METHODS**

**Twenty patients** (20 joints; 19 F and 1 M) suffering from symptoms of internal mechanical imbalance of the TMJ have been selected from the Outpatient Clinic of

Scoring		
<b>Pain on movement of the mandible</b>		
Criteria:	No pain on movement	0
	Slight pain on maximal mouth opening	1
	Pain on two or more movements	2
	Spontaneous or severe pain	5
<b>Temporo-mandibular Joint pain</b>		
Criteria:	No tenderness to palpation	0
	Discomfort to palpation	1
	Tenderness to palpation	2
	Severe tenderness to palpation	5
<b>Maximal mouth opening</b>		
Criteria:	≥ 40 mm	0
	≥ 35 mm	1
	≥ 30 mm	2
	< 30 mm	5
<b>Signs of Temporo-mandibular Joint noise and disc displacement</b>		
Criteria:	No joint noise	0
	Occasionally joint noise	1
	Palpable clicking	2
	Audible clicking	3
	Absence of previous clicking (closed block)	4
	Crepitation	5
<b>Muscle pain in masticatory muscles</b>		
Criteria:	No tenderness to palpation	0
	Discomfort to palpation	1
	Tenderness to palpation	2
	Severe tenderness to palpation	5

TAB. 1

**Clinical signs evaluation.**

– Clinical dysfunction of Helkimo’s Index, modified.

Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Mansoura University (Egypt) to undergo treatments.

The diagnosis was Anterior disc displacement with reduction (ADDWR), confirmed through clinical signs and symptoms. The patients' age ranged from 18 to 50 years, mean age 31 years.

– All patients were injected collagen (**MD-SMALL JOINTS** – Guna Spa, Milan) through 2 injections over 2 consecutive weeks (1 ml/week) (**FIG. 1**).

Clinical manifestations were evaluated according to Helkimo's Index modified for TMDs (Kurita *et al.*, 1997), regarding **1) pain on movement (P)** and **2) pain/muscle soreness on palpation (M)** (**TAB. 1**).

Each sign and symptom was scored from 0 to 5 according to clinical severity. Before the injection of MD-SMALL JOINTS every patient was informed about the aim of the study, procedures, and possible complications. Each patient was asked to sign the informed consent form.

– After appropriate disinfection of the skin overlying the TMJ with 10% Povidone-iodine solution and after plugging the external auditory meatus with a cotton pledge, auriculotemporal nerve was anesthetized (**FIG. 1**).

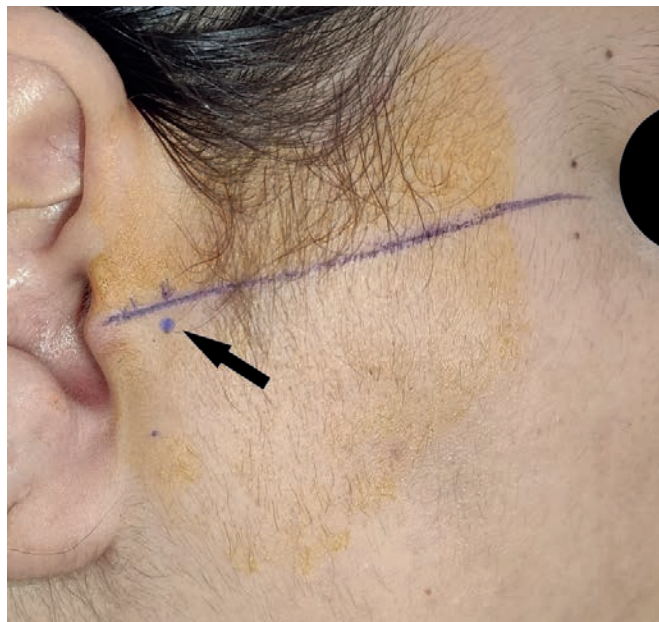
The superior joint space was localized 10 mm anterior to the tragus and 2 mm below the canthal tragus line; in this point was injected 1 ml of MD-SMALL JOINTS, drawn from a ready-made vial (2 ml) with a plastic disposable 3 cc 25G syringe (**FIGS. 2-4**).

Patients were required to eat a light diet and practice home physical therapy (application of moist heat and mandibular exercises 4 times daily for 1 month) as well as to take antibiotic: Amoxicillin + Clavulanic acid (Augmentin®) 625 mg tablets, 3 times/day for 5 consecutive days for prophylaxis of any joint space infection.



**FIG. 2**

**Needle insertion for auriculotemporal nerve block.**



**FIG. 3**

**Marking of the anatomical landmarks used for the injection in the superior auricular space of the TMJ and penetration point (black arrow).**

Ibuprofen (Brufen®) 600 mg tablets x 3/day, as an anti-inflammatory, was also prescribed in case of need.

Patients were evaluated at **1 week, 1 month** and **3 months** after the second injection, for improvement of signs and symptoms according to Helkimo's Index, modified for the evaluation of TMJ dysfunctions (Kurita *et al.*, 1997) regarding pain (**P**) and muscle pain and tenderness to palpation (**M**).

Finally, the collected data were analyzed to evaluate post-operative results.

## RESULTS

Regarding **pain on movement (P)**, there was a significant difference between all intervals ( $p = 0.00$ ). A significant improvement in pain ( $p$  value  $< 0.05$ ) was found when pre-operative pain was compared to that of 1 week ( $p = 0.001$ ), 1 month ( $p = 0.005$ ), and 3 months after the second injection.

– No significant improvement was found in the degree of pain when comparing in 1 week versus 1 month

FIG. 4

Needle insertion during the injection of MD-SMALL JOINTS.



( $p = 0.34$ ), 1 week vs 3 months ( $p = 0.11$ ) or 1 month versus 3 months ( $p = 0.18$ ) (TABLES 2-3).

As far as **muscle pain and tenderness to palpation (M)** are concerned, statistically, there was a significant difference among the pre-operative and all follow-up intervals ( $p = 0.00$ ).

A significant improvement in signs of muscular tenderness to palpation (M) ( $p < 0.05$ ) was noticed when pre-operative Muscular pain (M) was compared to that after 1 week ( $p = 0.00$ ), 1 month ( $p = 0.00$ ), and 3 months ( $p = 0.00$ ) from the second injection.

– No significant difference ( $p$  value  $> 0.05$ ) in the degree of pain when comparing 1 week versus 1 month ( $p = 0.00$ ), 1 week versus 3 months ( $p = 0.74$ ) or 1 month versus 3 months ( $p = 0.32$ ) (TABLES 4-5).

N	14
Chi-Square	20.532
df	3
Asymptotic significance (P value)	0.00

TAB. 2  
Test of Friedman for (P).

## DISCUSSION

Up to now, several preparations such as HA, corticosteroids, NSAIDs, PRF, PRP, and dextrose have been injected intra-articularly for the treatment of many TMDs.

- This study evaluated the effect of intra-articular injection of MD-SMALL JOINTS for the treatment of pain of anterior disc displacement associated to reduction.

– This is the first study to include intra-articular injection of collagen in the TMJ.

In previous studies Collagen Medical Devices had been used in other joints such as knee, ankle, shoulder, etc.

This study evaluated the effect of collagen injection according to Helkimo's Index, modified for TMDs (Kurita *et Al.*, 1997).

– This Index provides an evaluation of most of signs and symptoms of TMDs with scores that cover the different degree of severity of each factor. Moreover, this Index does not depend on the patients' feedback like the VAS scale, which covers only the pain variable and depends completely on the patient's evaluation of the degree of pain and, therefore, is less accurate.

Due to the lack of previous studies covering the injection of collagen in the TMJ, dosage was compared to that used in other joints, knee for instance.

– Reshkova *et Al.* (2016) used 2 ml of collagen in every knee injection. Since the width of the knee joint space is nearly double that of the TMJ [knee JSW medial and lateral is 4.7 mm and 5.6 mm respectively (Anas *et Al.*, 2013); TMJ joint space range from 2 mm to 3.2 mm (Mahmood *et Al.*, 2015)], the dose of collagen used in this study was half of that used in the knee (1 ml/treatment). The number of injections administered was equal to 2.

Besides, the fact that 95.0% of patients are females and 51.7 % of patients were aged from 18 to 30 years, is compliant with what reported by Bagis *et Al.* (2012) and Bueno *et Al.* (2018).

These Authors have – in fact – referred an increase of TMDs in females more than in males, especially in patients ranging between 30 and 40 years of age.

Regarding pain (P), patients showed a significant improvement, coherent with the results reported by Hynes (2002), Friedrichs *et Al.* (2007), and Del Nogal *et Al.*, (2012); they all described the collagen fibers anisotropy and its crucial role in force distribution and transmission to the fibroblasts which forms collagen itself and helps in Tissue repair.

– The results of this study confirm the efficacy and tolerability of the intra-articular injections of Collagen Medical Devices (Milani, 2019).

Concerning muscle tenderness (M), it's worth mentioning that the results which showed significant improvement confirm what reported by Ayesh *et Al.* (2008); i.e., painful TMJ increase skin and muscle sensitivity of the TMJ area, as well as finger-applied pressure stimuli.

These results are also confirmed by Tanaka *et Al.* (2008) who proposed that chronic TMJ pain leads to reflex masticatory muscle spasm.

Intervals	Mean Rank		Z value	P value
	Positive	Negative		
Pre-operative (P) vs 1 week (P)	0.00	6.50	-3.18	0.001
Pre-operative (P) vs 1 month (P)	0.00	5.00	-2.81	0.005
Pre-operative (P) vs 3 months (P)	0.00	4.50	-2.64	0.008
1 week (P) vs 1 month (P)	5.00	2.00	-0.097	0.34
1 week (P) vs 3 months (P)	4.50	1.50	-1.62	0.11
1 month (P) vs 3 months (P)	1.50	0.00	-1.34	0.18

TAB. 3

Ranks test (Wilcoxon) and relevant statistical significance for pain improvement in different intervals according to Helkimo's Index, modified.

Wang *et Al.* (2004) mentioned that patients with anterior disc displacement without reduction showed improvement in muscle tenderness after injection of Lidocaine in TMJ. Therefore, reduction of muscle tenderness and sensitivity can be attributed to the reduction of TMJ pain.

– We think that the limitations of this study are **1)** a relatively small sample (20 patients), **2)** lack of knowledge of the appropriate dose and number of collagen injections, due to the absence of previous use of collagen in the treatment of TMJ disorders.

### CONCLUSIONS

The positive results of our study open the doors to further investigations on intra-articular injection of collagen in TMJ and the possible use of MD-SMALL JOINTS in other types of internal mechanical imbalance or other TMDs. ■

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N	14
Chi-Square	21.217
df	3
Asymptotic significance (P value)	0.00

TAB. 4

Test of Friedman for (M).

TAB. 5  
Ranks test (Wilcoxon) and relevant statistical significance for pain/muscle soreness on palpation (M) in different intervals according to Helkimo's Index, modified.

Intervals	Mean Rank		Z value	P value
	Positive	Negative		
Pre-operative (M) vs 1 week (M)	0.00	6.00	-3.21	0.00
Pre-operative (M) vs 1 month (M)	0.00	5.00	-2.72	0.00
Pre-operative (M) vs 3 months (M)	0.00	4.50	-2.60	0.00
1 week (M) vs 1 month (M)	3.00	3.00	-0.45	0.66
1 week (M) vs 3 months (M)	4.00	3.00	-0.33	0.74
1 month (M) vs 3 months (M)	1.00	0.00	-1.00	0.32

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#### first author

**Dr. Muhammad Ibrahim Abdulhalim  
Muhammad Sakr**

– Outpatient Clinic of Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Mansoura University  
Mansoura, Egypt