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Clinical Evaluation of Intra-Articular Injection of Chondroitin Sulfate and Sodium Hyaluronate in the Management of Degenerative Osteoarthritis of Temporomandibular Joint

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Abstract

AIM: This study aims to evaluate the effectiveness of intra-articular injection of chondroitin sulfate and sodium hyaluronate in cases of temporomandibular joint (TMJ) degenerative osteoarthritis.

MATERIAL AND METHODS: Thirty patients ASA I of both sexes, who were selected from outpatient clinic of Oral Surgery Department, Faculty of Dentistry – Suez Canal University, complaining of painful TMJ, presence of unilateral or bilateral TMJ pain, impairment of jaw movements, and joint sounds. Clinical examination was performed to all patients and pre-operative measurements of visual analog scale (VAS) for morning pain, pain with movement and spontaneous pain, maximum mouth opening, and presence or absence of clicking. Patients were randomly divided into two groups; (a) **Study group** consisted of 15 patients, they had intra-articular injection of chondroitin sulfate and sodium hyaluronate once weekly for 3 weeks and (b) **control group** consisted of 15 patients, they had intra-articular injection of sodium hyaluronate once weekly for 3 weeks. Post-operative measurements of VAS for previous pain types, maximum mouth opening, and clicking were obtained at 1 month, 3 months, and 6 months post-injection.

RESULTS: There was a statistically significant reduction of all types of pain in the study group compared to the control group at all time intervals ($p \leq 0.05$), for maximum mouth opening, there was a significant improvement in mouth opening in the study group for all time intervals ($p \leq 0.05$), but for the clicking, there was not statistically significant difference between the study and control groups after 1 month, 3 months, and 6 months. The difference between groups was barely statistically significant ($p = 0.05$).

CONCLUSION: Intra-articular injection of a combination of chondroitin sulfate and sodium hyaluronate is an effective tool in reducing pain, clicking, limited mouth opening, and other symptoms associated with degenerative TMJ diseases.

Introduction

Temporomandibular Joint disorders (TMD) are defined as a group of clinical problems involving the masticatory muscles, the temporomandibular joints (TMJ) and associated structures, or both. Articular disorders include disk displacement disorders, arthritic or degenerative changes, and neoplasm [1]. Degenerative arthritis is the most common form of arthritis, usually affecting the hands, feet, spine, knees, and TMJ as well, it is also known as degenerative joint disease, it is a type of arthritis caused by inflammation, breakdown, and degeneration of the cartilage of the joints [2]. Degenerative joint arthritis has a multifactorial etiology, risk factors include age, genetics, trauma (repetitive adverse loading, overt jaw trauma, and prolonged micro trauma), disturbances of joint or muscle (internal derangements, inadequate muscle strength, and ligament laxity), and systemic conditions (generalized osteoarthritis, idiopathic degenerative process, and congenital and developmental abnormality) [3], [4], [5]. The most common symptom of any arthritic TMJ condition is painful joints, loss of joint function, limited mouth opening, joint instability, and clicking (depending on the stage of TMD) late stages most probably do not have clicking sounds [3]. Much of our current understanding of disease processes in the temporomandibular joint is based on the study of other articular joints. Management of degenerative arthritis has only symptom-modifying effects and a few structure-modifying effects [6].

Many studies have shown that non-surgical treatment can effectively be used to treat patients with osteoarthritis [7]. Treatment includes physical therapy, pulsed electrical stimulation, pharmacological, topical ointments, supplements, steroid injections, hyaluronic acid (HA) injections, and acupuncture. Early initiation of concomitant non-surgical therapies offers best outcome for long-term management [3]. Hyaluronic acid is a polysaccharide that is the main constituent of cartilage and synovial fluid; it is responsible for the mechanical

properties of the joint by allowing shock absorption, lubrication, and cartilage protection [8]. The results of several studies showed that intra-articular injection of HA has been proven to reduce pain in approximately 70% of patients with osteoarthritis of the knee, pain reduction was better than placebo in most studies and equal to nonsteroidal anti-inflammatory drugs (NSAIDs) [9], [10]. Chondroitin sulfate (CS) is a major component of the extracellular matrix of many connective tissues, including cartilage, bone, skin, ligaments, and tendons [11], it has been used for medicinal purposes for over 40 years. CS is sold as over-the-counter dietary supplement in North America and is a prescription drug under the regulation of the European Medicine Agency in Europe [12] CS is an inhibitor of extracellular proteases involved in the metabolism of connective tissues and stimulates proteoglycan production by chondrocytes *in vitro*; it also inhibits cartilage cytokine production and increases the intrinsic viscosity of the synovial liquid [13]. Some authors found that intra-articular injection of chondroitin sulfate stimulated the chondrocyte metabolic activity and was possibly helpful to decrease the degenerative process [11]. Combining hyaluronic acid with chondroitin sulfate was found to have a positive effect on joint bony structures, cartilage matrix production, and chondrocyte proliferation by articular chondrocytes, along with the known effects on each component alone [14], [15], [16].

Materials and Methods

Study design

This study was a randomized clinical trial with a 1:1 allocation ratio. The methods were not changed after trial initiation.

Participants, eligibility criteria, and settings

The study was reviewed and approved by the Institutional Review Board at Faculty of Dentistry – Suez Canal University in Egypt (approval number 76/2018). The participants for this study were recruited from patients attending postgraduate outpatient clinic of oral surgery department, who are complaining of painful TMJ, presence of unilateral or bilateral TMJ pain during palpation, joint sounds, and impairment of jaw movements. All subjects who agreed to participate in the study signed a consent form for participation after clarifying the duration, number of visits, and risks and benefits of the intervention. Subjects were selected based on the inclusion criteria; age ≥ 16 years and ≤ 55 years.

Exclusion criteria were; previous history of allergy to any of the drugs administered during the treatment, any systemic diseases that could jeopardize the study (e.g., systemic rheumatoid arthritis and bleeding disorders), children, patients who had TMJ surgery, direct trauma or fracture of TMJ, and pregnancy.

Sample size

Based on the paper by Rivera *et al.*, 2016 [15], who reported 77% pain reduction by intra-articular injection of sodium hyaluronate-chondroitin sulfate, a total sample size of 30 patients were sufficient with power of 80% and 5% significance level. The sample size was calculated by the application G* power program.

Intervention

Pre-operative phase

Clinical examination was performed to all patients, and a checklist was designed based on questions asked to the patient to collect required data related to symptoms and clinical examination [17].

Pre-operative measurements were:

1. Pain score (VAS) was obtained from the patients. The VAS values were evaluated using a scale with two anchor points; 0 being no pain and 10 being the worst imaginable pain, VAS was measured for pain with movement, spontaneous pain, and morning pain.
2. Presence or absence of joint sound (clicking).
3. Maximum mouth opening was measured as the distance in millimeters between the incisal edges of upper and lower central incisors using digital caliper.

Operative phase

Patients were divided into two groups

1. Study group: Formed of 15 patients, they were injected (intra-articular) with Arthrum HCS 1 ML in the form of 2 mL syringe: Chondroitin sulfate 40 mg and sodium hyaluronate 40 mg (Pack of $3X_{2\ mL}$ syringes) (LCA Pharmaceutical-France) once per week for 3 weeks (Figure 1).
2. Control group: Formed of 15 patients, they were injected (intra-articular) with sodium hyaluronate (HYALGAN 20 mg/2 mL syringe, Fidia Farmaceutici S.p.A., Italy), once per week for 3 weeks (Figure 2).

Technique

- We employed the method suggested by McCain *et al.* [18] to approach superior joint space. A line was drawn from the middle of the tragus to the outer canthus and entry point marked

Figure 1: Sodium hyaluronate in the form of Hyalgan 20 mg/2 mL syringe, Fidia Farmaceutici S.P.A., Italy

along this canthotragal line. The injection point which corresponds to the glenoid fossa was marked 10 mm from the mid-tragus and 2 mm below the line (Figure 3a).

- Skin was disinfected with povidone-iodine at the entry point.
- Topical anesthesia was achieved with lidocaine (Xylocaine Spray®, AstraZeneca Ltd., UK, with nozzle attached). Each spray delivers 10 mg of lidocaine surface, thus anesthetizing the soft tissues over the joint.
- Arthrum/Hyalgan syringe was inserted through entry point into joint space then injection of 1 ML/0.5 ML solution respectively over 6 s (Figure 3b).

Post-operative phase

Follow-up to both groups at 1 month, 3 months, and 6 months – post-injection – for the following:

1. Pain score (VAS) for morning pain, spontaneous pain, and pain on movement.
2. Presence or absence of joint sound (clicking).
3. Maximum mouth opening.

Figure 2: (a) Arthrum package and (b) the 2 mL syringe containing 40 mg chondroitin sulfate and 40 mg sodium hyaluronate

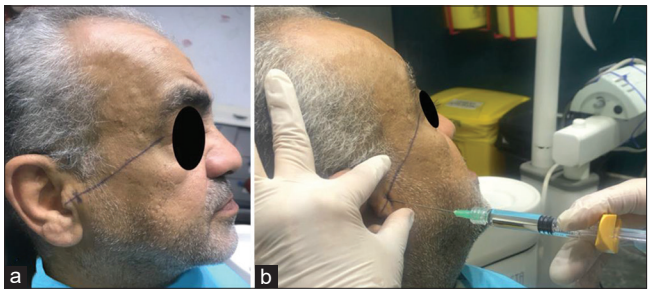

Figure 3: (a) McCain landmarks to locate superior joint space, (b) Point of injection

Statistical analysis

Statistical analysis was performed with SPSS 20® and Microsoft Excel 2016. Data were explored for normality using Shapiro–Wilk and Kolmogorov–Smirnov normality test which revealed that values were parametric data. Quantitative data were presented as means and standard deviation. Comparisons between groups were performed by independent t-test, while repeated measures ANOVA test was used to compare different observation times within the same group. Statistical significance was established as $p \leq 0.05$.

Results

Thirty patients, 17 (56.6%) females and 13 (43.3%) males, received the planned intervention, their ages were ranging from 19 to 55 years (mean = 33.37 ± 10.87). They were suffering of TMJ pain, clicking, and limited mouth opening.

Demographic characteristics

The study group consisted of 10 females and five males, with age ranging from 19 to 55 years (mean = 33.5 ± 12.7), while the control group consisted of seven females and eight males, with age ranging from 19 to 52 years (mean 33.2 ± 9.14). The difference between groups regarding age and gender was not statistically significant ($p = 0.936$ and $p = 0.269$, respectively). There was no significant difference between groups regarding marital status ($p = 0.439$) and education ($p = 0.336$), (Table 1). Patients suffered from TMJ pain, clicking, and limited mouth opening. In the study group, 53.3% of patients (n = 8) were suffering of the right TMJ, while 26.7% (n = 4) had both TMJs symptoms, and 20% (n = 3) had symptoms at the left TM, in comparison to 60% (n = 9), 26.7% (n = 4), and 13.3% (n = 2) in the control group (Figure 4).

Pain score (VAS)

Results of VAS pain score are summarized in Tables 2-4.

Table 1: Demographic characteristics of the control and study groups (age, gender, marital status, and education) of patients

Patient	Age		Gender		Marital Status		Education	
	Study	Control	Study	Control	Study	Control	Study	Control
1	45	43	F	F	Married	Married	Post graduate	Post graduate
2	19	22	F	F	Not Married	Not Married	Under graduate	Under graduate
3	23	52	F	M	Not Married	Married	Post graduate	Post graduate
4	22	43	F	F	Not Married	Married	Under graduate	Post graduate
5	50	34	M	M	Married	Married	Post graduate	Post graduate
6	34	33	M	M	Married	Married	Post graduate	Post graduate
7	20	36	F	F	Not Married	Married	High school	Post graduate
8	41	29	F	F	Married	Married	Post graduate	Post graduate
9	19	30	F	M	Not Married	Not Married	Under graduate	Post graduate
10	55	28	M	F	Married	Married	Post graduate	Post graduate
11	32	19	F	M	Married	Not Married	Post graduate	Under graduate
12	18	44	F	M	Not Married	Married	High school	Post graduate
13	45	32	F	M	Married	Married	Post graduate	Post graduate
14	36	23	M	F	Married	Not Married	Post graduate	Under graduate
15	44	30	M	M	Married	Married	Post graduate	Post graduate
Mean ± SD	33.53 ± 12.7	33.2 ± 9.14						
No. (%)	Females: 10 (66.7%)		Males: 5 (33.3%) Females: 7 (46.7%)	Males: 8 (53.3%) Not married: 6 (40%)	Married 9: (60%) Not married: 4 (26.7%)	Married: 11 (73.3%) Undergrad: 3 (20%) High school: 2 (13.3%)	Postgrad. 10 (66.7%) Undergrad. 3 (20%) -	Postgrad. 12 (80%)
P value	0.936 ns		0.269ns		0.439 ns		0.336 ns	

Comparison between groups regarding different types of pain

- At pre-operative; pain with movement recorded the highest value (7.87 ± 0.74) in both groups, while spontaneous pain was slightly higher in the study group (4.07 ± 0.8) compared to control (3.87 ± 0.74) and morning pain showed almost equal means in both groups (4.07 ± 0.8).

Table 2: Mean values of visual analog scale pain scores for pain with movement at pre-operative, days 30, 90, and 180 post-injection for the study and control groups

Parameter	Pain with movement			
	Mean ± SD		*t*	p value between groups
	Study group	Control group		
Pre-operative	7.87 ± 0.74	7.87 ± 0.74	28	1.0 NS
Day 30	5.27 ± 0.80	7.20 ± 0.86	6.37	0.000*
Day 90	3.47 ± 0.83	7.20 ± 0.86	12.06	0.000*
Day 180	1.6 ± 0.51	6.73 ± 1.16	15.67	0.000*
F	265.1	465.8		
p value within group	<0.0001*	<0.0001*		

Significance level p ≤ 0.05. *Significant. NS: Non-significant, SD: Standard deviation. p value of difference between groups was calculated using t-test for age and Chi-square test for qualitative data.

- At day 30, pain with movement recorded a significantly higher value in the control group (7.2 ± 0.86), in comparison to 5.27 ± 0.8 in the study group (p = 0.000). Moreover, spontaneous pain recorded a significantly higher value in the control group value (3.27 ± 0.8), in comparison to 2.4 ± 0.63 in the study group (p = 0.003). Morning pain showed a significantly higher value in the control group (3.73 ± 0.7), in comparison to 2 ± 0.54 in the study group (p = 0.000).
- At day 90, pain with movement recorded a significantly higher value in the control group (7.2±0.86), in comparison to 3.47 ±0.83 in the study group (p=.000). Moreover, spontaneous pain recorded a significantly higher value in the control group value (3.27±0.8), in comparison to 1.20±0.78 in the study group (p=.000). Morning pain showed a significantly higher value in the control group (3.73±0.7), in comparison to 1.2 ±0.41 in the study group (p=0.000).
- At day 180, pain with movement recorded a significantly higher value in the control group (6.73±1.16), in comparison to 1.6 ±0.51 in the study group (p=.000). Moreover, spontaneous pain recorded a significantly higher value in the control group value (3.27±0.8), in comparison to

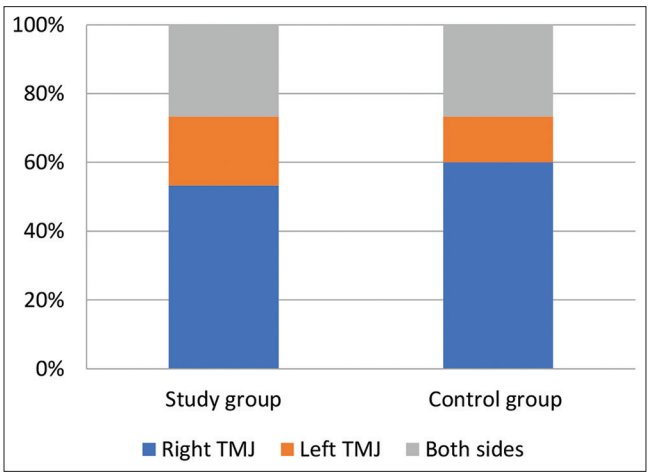

Figure 4: Bar chart illustrating affected joint in study and control groups

Table 3: Mean values of visual analog scale pain scores for the spontaneous pain at pre-operative, days 30, 90, and 180 post-injection for the study and control groups

Parameter	Spontaneous pain score			
	Mean ± SD		*t*	p value between groups
	Study group	Control group		
Pre-operative	4.07 ± 0.8	3.87 ± 0.74	28	0.484 NS
Day 30	2.40 ± 0.63	3.27 ± 0.8	3.29	0.003*
Day 90	1.20 ± 0.78	3.27 ± 0.8	7.19	0.000*
Day 180	0.40 ± 0.51	3.72 ± 0.8	11.73	0.000*
F	128.4	268.3		
p value within group	< 0.0001*	< 0.0001*		

Significance level p ≤ 0.05. *Significant. NS: Non-significant, SD: Standard deviation.

Table 4: Mean values of visual analog scale pain scores for the morning pain at pre-operative, days 30, 90, and 180 post-injection for the study and control groups

Parameter	Morning pain score			
	Mean ± SD		*t*	p value between groups
	Study group	Control group		
Pre-operative	4.07 ± 0.80	4.07 ± 0.8	28	1.0 NS
Day 30	2.00 ± 0.54	3.73 ± 0.7	7.6	0.000*
Day 90	1.20 ± 0.41	3.73 ± 0.7	12.02	0.000*
Day 180	0.60 ± 0.51	3.73 ± 0.7	13.99	0.000*
F	93.06	905.2		
p value within group	< 0.0001*	> 0.0001*		

Significance level p ≤ 0.05. *Significant. NS: Non-significant, SD: Standard deviation.

0.4±0.51 in the study group (p=.000). Morning pain showed a significantly higher value in the control group (3.73 ± 0.7), in comparison to 0.6 ± 0.51 in the study group (p = .000).

Effect of time within the same group

Repeated measures ANOVA test was used to compare pain scores at pre-operative and after 6 months for all types of pain (spontaneous, movement, and morning) and revealed a statistically significant difference by time within the same group for each type of pain (p<0.0001).

Maximum mouth opening

Results of maximum mouth opening (cm) are summarized in Table 5.

Table 5: Mean value of maximum mouth opening at pre-operative, days 30, 90, and 180 post-injection for both groups

Parameter	Maximum mouth opening (cm)			
	Mean ± SD		*t*	p value between
	Study group	Control group		groups
Pre-operative	3.87 ± 0.55	3.27 ± 0.56	2.95	0.006*
Day 30	4.00 ± 0.49	3.33 ± 0.54	4.62	0.000*
Day 90	4.25 ± 0.37	3.51 ± 0.54	6.55	0.000*
Day 180	4.42 ± 0.35	3.93 ± 0.55	9.12	0.000*
F	21.15	1.47		
p value within group	<0.0001*	0.219 NS		

Significance level p ≤ 0.05. *Significant. NS: Non-significant, SD: Standard deviation.

Comparison between groups

- At pre-operative; a significantly higher value in study group value (3.87 ± 0.55 cm), in comparison to 3.27 ± 0.56 cm in the control group (p = 0.006).
- At day 30, a significantly higher value in the study group value (4±0.49 cm), in comparison to 3.1 ± 0.57 cm in the control group (p = 0.000).
- At day 90, a significantly higher value in the study group value (4.25 ± 0.37 cm), in comparison to 3.3 ± 0.54 cm in the control group (p = 0.000).
- At day 180, a significantly higher value in the study group value (4.42 ± 0.35 cm), in comparison to 3.93 ± 0.55 cm in the control group (p = 0.000).

Effect of time within the same group

Repeated measures ANOVA test was used to compare maximum mouth opening at baseline and different follow-up times and revealed a statistically significant difference by time (p < 0.0001) in the study group, whereas there was no significant difference by time in the control group (p = 0.219).

Presence or absence of joint sound (clicking)

Results of joint sound (clicking) are summarized in Table 6.

Comparison between groups

- At pre-operative, jaw clicking was observed in 66.7% of the patients in the study group, in comparison to 73.3% in the control group. The difference between groups was not statistically significant (p = 0.69).
- At day 30, the percentage of patients with jaw clicking decreased to 53.35% in the study, but remained constant at 73.3% in the control group. The difference between groups was not statistically significant (p = 0.256).
- At day 90, the percentage of patients with jaw clicking further decreased to 40% in the study group, but remained constant at 73.3% in the control group. The difference between groups was not statistically significant (p = 0.065).
- At day 180, the percentage of patients with jaw clicking further decreased to 20% in the study group, in comparison to 53.3% in the control group. The difference between groups was barely statistically significant (p = 0.05).

Effect of time within the same group

In the study group, a statistically significant difference in incidence of jaw clicking was observed throughout the study (from baseline to day 180) (p = 0.0033). However, in the control group, the difference by time was not statistically significant (p = 0.688).

Discussion

Temporomandibular joint disorders are a heterogeneous group of pathologies that cause

Table 6: Number and percent of patients presenting with jaw clicking at pre-operative, days 30, 90, and 180 post-injection for both groups

Time	Study group		Control group		χ^2	p
	Jaw clicking, *n* (%)	No jaw clicking, *n* (%)	Jaw clicking, *n* (%)	No jaw clicking, *n* (%)		
Pre-operative	10 (66.7)	5 (33.3)	11 (73.3)	4 (26.7)	0.159	0.69 NS
Day 30	8 (53.3)	7 (46.7)	11 (73.3)	4 (26.7)	1.92	0.256 NS
Day 90	6 (40)	9 (60)	11 (73.3)	4 (26.7)	3.39	0.065 NS
Day 180	3 (20)	12 (80)	8 (53.3)	7 (46.7)	3.90	0.05*
χ^2	8.64		2.26			
p	0.0033*		0.688 NS			

Significance level p ≤ 0.05, *Significant. NS: Non-significant. Harms: Negative outcomes were not reported by any patients during the trial.

complaints of pain in masticatory area, limitation of jaw movements, headache radiating to the lateral neck, or clicking sounds on jaw opening or closing. The symptoms are caused by the heavy stress on the joint or on neighboring structures [3]. In the present demographic data, females were relatively more than male participants (57% and 43%, respectively) who agree with multiple studies' findings where females had TMD signs and symptoms more frequently than males [19], [20]. The present study showed that more than half of patients (56.6%) who were affected by TMD had symptoms on the right side. Armstrong and Oldham [21] showed that the dominant hand was slightly stronger than the non-dominant hand and Čular *et al.* [22] showed that right-handed persons showed a high prevalence in the right body movements. Thus, there could be a relation between the dominant body side in patients and TMJ pain side.

In this clinical study, we employed the method suggested by McCain *et al.* [18] to approach superior joint space, for intra-articular injection. The superior space is a larger cavity compared with the lower space, and injection into the upper space is easier to handle. That is why the superior space injection approach has been popular for many years [23]. However, Kondoh *et al*. pointed out that the articular disk had a higher prevalence of morphologic changes on the inferior surface than the superior surface and that there were specific differences between the two disk surfaces in chronic internal derangement of TMJ [24], but the main point is that inferior space injection was believed to be a difficult procedure because of the small volume and hidden location, although the inferior space of the TMJ is narrow, especially when the condyle seats under the fossa, it will expand its volume when opening the mouth, providing a chance for puncturing into the space [25].

Intra-articular drug injections can be applied alone or following arthrocentesis or arthroscopic surgery; however, the effectiveness of intra-articular drug injections following arthrocentesis is still controversial [26], in this study, we applied injection alone and we had favorable results clinically.

To the best of our knowledge, there is no clinical study that tested intra-articular injection of chondroitin sulfate into TMJ, most of studies were either experimental [13], [27], [28], [29] or clinical through using chondroitin sulfate as an oral supplement and they had favorable results in terms of pain, maximum mouth opening, and clicking [30], [31], [32]. Furthermore, none of these studies have tested chondroitin sulfate solely, usually, it was used in combination with hyaluronic acid or with glucosamine hydrochloride [15], [27], [28], [30], [32], in our study, we tested injection of chondroitin sulfate in combination with sodium hyaluronate with the study group.

We investigated three types of pain in the present study; morning pain, movement pain, and spontaneous pain, they were evaluated at baseline, after 1 month, 3 months, and 6 months. Throughout the study duration; movement pain recorded the highest value, while morning and spontaneous pain had relatively similar values. For the control group who had only sodium hyaluronate injection, spontaneous pain and pain with movement had been significantly reduced after 6 months ($p < 0.0001$), these findings agree with El-Hakim and Elyamani [33], [34] and Gencer *et al.* [34] who found that the hyaluronate acid injection produced significantly better pain scores compared to other anti-inflammatory agents used, and they referred this to the effect of HA of reducing the levels of inflammatory mediators in synovial fluid IL1β and IL6 levels, also several studies reported persistent beneficial effects of the intra-articular application of HA [35], [36]. Similarly, De Riu *et al.* [37] reported significant decreases in pain in patients with internal derangement of the TMJ who received arthrocentesis followed by sodium hyaluronate injection. Henrotin *et al.* [14] who injected a combination of hyaluronic acid and chondroitin sulfate intra-articular in knee joint, they found that patients reported being "very satisfied of the treatment" at week 12 post-injection, while in our study, the most significant difference in pain scores were at week 6 post-injection compared to baseline, yet similar satisfaction had been reported with our study group patients who had the same treatment.

Maximus mouth opening was measured at baseline and at days 30, 90, and 180 post-injection, and the mean value at these timings revealed a statistically significant difference by time ($p < 0.0001$) for the study group; on the other hand, it was non-significant for the control group, these findings were not in agreement with studies that used arthrocentesis for improving TMD symptoms [38], [39] as well as those who performed intra-articular injections which could be hyaluronic acid or corticosteroids [34], [40] where both of them gave satisfying results in terms of reducing pain and improving function, and there was no statistically significant difference between both treatments.

In the present study, we compared mean value of clicking at baseline and different follow-up times for both groups, the results revealed a statistically significant difference at baseline and after 6 months post-injection ($p = 0.0351$) for the study group, although, there was no significant difference between mean value at baseline versus day 30 ($p = 0.865$) and day 90 ($p = 0.370$), Ali B. [41] who performed three cycles of intra-articular injections of 0.6 ML sodium hyaluronate weekly for 3 successive weeks found that highly significant difference in clicking before and after injections of hyaluronic acid, also he concluded that intra-articular injection of HA is a safe and effective treatment modalities of TMDs including clicking, although for the present control group, we injected 1 ML of sodium hyaluronate for three cycles, jaw clicking was observed in 73.3% of the patients at pre-operative and day 30 and day 90, this percentage decreased to 20% at day 180 but Chi-squared test revealed a non-statistically significant difference in incidence of jaw clicking at baseline and at day 180 ($p = 0.0033$).

Conclusion

Up to the current knowledge, this is the first study to inject a combination of hyaluronic acid and chondroitin sulfate intra-articular in the temporomandibular joint, and it showed that it is an effective tool in reducing pain, clicking, limited mouth opening, and other symptoms associated with degenerative TMJ diseases. It is a minimally invasive application with minimum to almost no complications.

Recommendations

- Arthrum could be recommended as a safe intra-articular injection for TMJ degenerative diseases to control clinical symptoms as pain, clicking, and limited mouth opening.
- This study can be repeated with larger sample size and longer duration of follow-up.

Data Availability

The data that support the findings of this study are available from the corresponding author on reasonable request.

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