Journal of Cranio-Maxillo-Facial Surgery 47 (2019) 1720–1727

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Comparison of treatment efficacy between hyaluronic acid and arthrocentesis plus hyaluronic acid in internal derangements of temporomandibular joint

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ARTICLE INFO

Article history:
Paper received 17 January 2019
Accepted 22 July 2019
Available online 25 July 2019

Keywords:
Temporomandibular joint
Arthrocentesis
Treatment outcome

ABSTRACT

The aim of the study was to compare the effectiveness of hyaluronic acid (HA) injection and arthrocentesis plus HA injection for treating disc displacement with reduction (DDwR) and disc displacement without reduction (DDwoR). In this randomized clinical trial, patients were divided into 2 main groups: group I (DDwR) and group II (DDwoR). Sub-groups were made depending on allocated treatment: group Ia (arthrocentesis plus HA), group Ib (single HA), group Ic (control), group IIa (arthrocentesis plus HA), group IIb (single HA), and group IIc (control). The primary outcome variable was maximum pain on chewing, while maximum pain at rest, maximum non-assisted and assisted mouth opening, chewing efficiency, temporomandibular joint (TMJ) sounds, quality of life, treatment tolerability, and treatment effectiveness were secondary outcomes. The influences of individual study variables (gender, involved side, and duration of symptoms) on clinical outcomes were also examined. The study consisted of 116 TMJs of 90 patients (n = 45 in both main groups, TMJs = 58) aged 15–82 years. At the 6-month follow-up, improvement in all parameters, except for TMJ sounds, was recorded in all treatment groups, with no improvements in control groups. Notably, arthrocentesis plus HA showed superior improvement in chewing efficiency ($p = 0.041$) and quality of life ($p = 0.047$) of group I and quality of life ($p = 0.004$) in group II, compared to single HA. Furthermore, the duration of symptoms correlated with clinical outcomes. Both procedures successfully improved the symptoms of DDwR and DDwoR patients, but arthrocentesis plus HA injection seemed superior.

1. Introduction

Temporomandibular joint (TMJ) internal derangements are the most common form of TMJ disorders (Emshoff and Rudisch, 2007; Tuncel, 2012). Internal derangements are conditions in which the articular disc displaces from its original position on the condylar head. Disc displacement with reduction (DDwR) and disc displacement without reduction (DDwoR) are the most prevalent forms of TMJ disc displacements (Young, 2015; Zhang et al., 2009; Korkmaz et al., 2016). The etiology of TMJ disorders are not fully understood and could be related to risk factors, including parafunctional habits, occlusion, orthodontic treatment, emotional stress, trauma, genetic and psychosocial factors, age, and gender (Bagis et al., 2012; Chisnoiu et al., 2015). The internal derangements are associated with clinical findings such as pain, joint sounds, limited mouth opening, and chewing disability. These symptoms may be present alone or in combination with one another (Emshoff and Rudisch, 2007; Sharma et al., 2013; Zhang et al., 2009).

Management of TMJ internal derangements has always been a therapeutic challenge for maxillofacial surgeons. Approximately 25% of the entire population suffers from TMJ internal derangements (Guarda-Nardini et al., 2007; Neeli et al., 2010; Zhang et al., 2009). Initially, these conditions can be managed conservatively by employing techniques such as occlusal splint therapy, physiotherapy, pharmacotherapy, and occlusal treatments (Guarda-Nardini et al., 2007; Neeli et al., 2010). If conservative management fails, minimally invasive (sodium hyaluronate or

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https://doi.org/10.1016/j.jcms.2019.07.030
1010-5182/

corticosteroid infiltrations and arthrocentesis) and invasive treatments (arthroscopy, arthroplasty, arthrotomy, discectomy, condylotomy) are performed (Guarda-Nardini et al., 2007; Miloro and Henriksen, 2010; Neeli et al., 2010; Sharma et al., 2013).

Arthrocentesis is considered the first line of surgical intervention in patients with TMJ internal derangements, who do not respond to conservative treatment. Arthrocentesis breaks down adhesions within the joint and removes inflammatory mediators (cytokines and interleukins) that cause chronic pain. Alleviating TMJ pain leads to improvement in mouth opening and dysfunction (Neeli et al., 2010; Sharma et al., 2013).

Various pharmacological agents such as non-steroidal anti-inflammatory drugs, corticosteroids, opioids, local anesthetic agents, and sodium hyaluronate have been intra-articularly injected to alleviate TMJ pain and dysfunction (Guarda-Nardini et al., 2007; Manfredini et al., 2012; Sipahi et al., 2015). Viscosupplementation with sodium hyaluronate has also become an option for the management of symptoms in the clinical setting, with the knowledge that impaired joint lubrication could be a risk factor for TMJ internal derangements (Guarda-Nardini et al., 2007; Manfredini et al., 2012; Sharma et al., 2013). Intra-articular hyaluronic acid (HA) injection alone or after arthrocentesis provides long-term palliative effects on subjective symptoms and clinical signs of TMJ pain (Neeli et al., 2010; Sharma et al., 2013; Korkmaz et al., 2016).

The positive effects of HA injection and arthrocentesis have been proven in the treatment of TMJ disorders. However, limited data is available that collates efficacy of single HA injection and arthrocentesis plus HA injection together. We aimed to rule out which treatment method is most suitable for DDwR or DDwoR. Therefore, the present study was designed to compare the effect of arthrocentesis plus HA injection and single HA injection on clinical outcome variables in patients with TMJ internal derangements.

2. Material and methods

2.1. Study design

The authors designed and implemented a prospective clinical trial. The study population consisted of patients with TMJ DDwR or DDwoR, treated at the Department of Oral and Maxillofacial Surgery of Karadeniz Technical University Faculty of Dentistry (Trabzon, Turkey) between 2015 and 2016. Patients with unilateral or bilateral TMJ pain, TMJ sounds, and impaired jaw function for at least 6 months were included in this study. Criteria for inclusion were the diagnosis of DDwR and DDwoR according to symptoms, clinical signs, and radiographic findings (Hepguler et al., 2002). Magnetic resonance imaging was used to confirm the presence of DDwR or DDwoR in all patients. Patients were excluded if they had prior history of TMJ treatment (e.g., conservative therapy or surgery), congenital or inflammatory joint disease, serious systematic diseases, or were edentulous.

The present study followed the Declaration of Helsinki for medical protocols and ethics. The Karadeniz Technical University Institutional Review Board approved the study plan under protocol 2015/133. Patients were informed about the procedure, possible complications, and the materials used, and they signed a detailed written consent form.

2.2. Study variables

The treatment method for DDwR and DDwoR was the primary predictor variable, and arthrocentesis plus HA injection or single HA injection were treatment methods. The patients were divided into 2 main groups: group I (patients with DDwR) and group II (patients with DDwoR). Sub-groups were allocated according to the treatment methods: group Ia (arthrocentesis plus HA injection), group Ib (single HA injection), group Ic (control group), group IIa (arthrocentesis plus HA injection), group IIb (single HA injection), and group IIc (control group). Treatment methods were numerically coded on slips of a paper by an impartial observer who was not associated with the study. The numbers were chosen by the patients. This allowed random assignment of the subjects into the two groups. For ethical reasons, patients with DDwR or DDwoR diagnosis and chief complaints of TMJ pain, who refused any treatment for any reason, were assigned to the control groups. The control groups were self-selected.

The injection technique used in the present study was the single-needle technique suggested by Guarda-Nardini et al. (2008) The skin surface was disinfected with 10% povidone iodine solution. The needle insertion site was marked on the skin 10 mm anterior to the tragus and 2 mm below the cantho-tragal line. Articaine with epinephrine (1:100,000 ratio) was administered for local anesthesia (Ultracain D-S Forte, Aventis, Istanbul, Turkey). The patients' mouths were opened wider for better definition of the glenoid fossa, and a 22-mm gauge needle was inserted into the superior joint space using the anatomical landmarks. While the mouth was open, 2 mL of high molecular weight HA solution (Orthovisc, Anika Therapeutics, Bedford, MA) was injected into the superior joint space of the TMJ.

After disinfecting the preauricular area with povidone iodine, the insertion points of the needles for arthrocentesis were marked on the skin as described by Laskin (1998). The first needle was inserted 10 mm anterior to the tragus and 2 mm below the cantho-tragal line. The second needle was placed 3–4 mm in front of the first needle. Articaine with epinephrine was injected into the superior joint space for local anesthesia. Two 22-gauge needles were used for the arthrocentesis procedure. The joint was irrigated with a minimum of 250 mL Ringer's lactate solution. After the joint lavage was completed, 2 mL high molecular weight HA solution was injected through the posterior needle. After treatment, all patients were advised to rest the joint for 7 days and adhere to a soft diet.

The maximum pain on chewing was selected as the primary outcome variable to rate treatment effectiveness. The secondary outcome variables were maximum pain at rest, maximum non-assisted mouth opening (MNMO, pain-free opening), maximum assisted mouth opening (MAMO, when the examiner used moderate digital pressure to increase the degree of opening, if possible), subjective chewing efficiency, TMJ sounds, quality of life, treatment tolerability, and perceived treatment effectiveness.

Maximum pain at rest and maximum pain on chewing were measured on a 10-point visual analogue scale (VAS) with 0 indicating absence of pain and 10 indicating the worst pain ever. MNMO and MAMO were measured by the distance between the incisal edge of the upper and lower central incisors (in millimeters). Subjective chewing efficiency was also measured on a 0–10 VAS scale (0 being the worst efficiency ever and 10 the best efficiency ever). TMJ sounds were determined on a 3-point scale (0, absent; 1, slight; 2, severe indicating joint sound easily detected by another person). Patients were asked to rate their quality of life on a line ranging from 0 (worst possible life quality) to 100 (best imaginable life quality). Treatment tolerability and perceived treatment effectiveness were measured on a 5-point Likert-type scale (0 being the lowest and 4 the maximum values).

Six clinical parameters were recorded for each patient at the time of diagnosis and at the 6-month follow-up, and treatment tolerability and perceived treatment effectiveness were evaluated at the end of the follow-up period. The outcome parameters were recorded by the same clinician fully blinded to patient groups. To minimize bias related to the patients' knowledge of their joint

status, they received only a generic explanation about the potential benefit of the treatment approach.

The influences of gender, side involved (right, left, or right and left), and duration of symptoms (6–12 months, >12 months) on clinical outcomes were examined.

2.3. Statistical analysis

Statistical analysis was performed using SPSS for Windows 17.0 (SPSS, Inc, Chicago, IL). The normality of distribution was tested with Shapiro–Wilk test. For inter-group comparison of non-parametric data, the Kruskal–Wallis and Mann–Whitney U-tests with Bonferroni correction were used (if needed), and intra-group comparisons were analyzed using Wilcoxon signed rank tests. The X^2 and Spearman correlation tests were performed as necessary. For all comparisons, statistical significance was set at $p < 0.05$.

3. Results

A total of 116 TMJs of 90 patients (78 women, 12 men; age range, 15–82 years; mean age at baseline, 33.9 years) were enrolled in the study. Group I (DDwR) consisted of 45 patients (58 TMJs), of which 18 patients (23 TMJs) were in group Ia, 18 (22 TMJs) in group Ib, and 9 (13 TMJs) in group Ic. Group II (DDwoR) consisted of 45 patients (58 TMJS), of which 19 patients (23 TMJs) were in group IIa, 18 (25 TMJs) in group IIb, and 8 (10 TMJs) in group IIc. No complications or side effects related to treatment methods were observed in any patient.

Descriptive statistics, including study variables of the groups, are listed in Tables 1 and 2. The mean age, gender distribution, and affected TMJ characteristics (duration of symptoms and involved side) of participants were not significantly different between the groups ($p > 0.05$).

Table 3 presents the comparisons between the individual study variables and the primary outcome variable. In groups I and II, significant differences were found in the comparison between duration of symptoms >12 months and duration of symptoms 6–12 months for the maximum pain on chewing scores 6 months post-treatment ($R = 0.423$, $p = 0.002$ and $R = 0.419$, $p = 0.001$, respectively). However, no significant correlation was found between pain scores and gender or involved side at the 6-month follow-up ($p > 0.05$).

The results of comparisons between the primary predictor variables and the primary outcome variables are presented in Tables 4 and 5. In all treatment groups, significant improvement with respect to baseline values was achieved in the pain scores at the end of the follow-up. However, the pain level of both control groups did not change ($p > 0.05$). The maximum pain on chewing values for all treatment groups were significantly lower than the control groups ($p < 0.01$). Pain scores at the end of the treatment did not differ significantly between groups Ia and Ib, or between groups IIa and IIb ($p > 0.05$), although the improvement was slightly better in the arthrocentesis plus HA groups than in single HA injection groups.

Comparisons between individual study variables and secondary outcome variables are presented in Table 6. According to the results, in group I, significant differences were found between the duration of symptoms >12 months and duration of symptoms 6–12 months with respect to comparisons in chewing efficiency ($R = -0.467$; $p < 0.001$), treatment effectiveness ($R = -0.591$; $p < 0.001$), and quality of life ($R = -0.586$; $p < 0.001$), 6 months after treatment. In group II, significant differences were found, 6 months after treatment, between the duration of symptoms >12 months and duration of symptoms 6–12 months with respect to comparisons of MAMO ($R = -0.279$; $p = 0.034$), chewing efficiency ($R = -0.424$; $p = 0.001$), treatment effectiveness ($R = -0.446$; $p = 0.002$), and quality of life ($R = -0.608$; $p < 0.001$). However no significant correlation was found between secondary outcomes and gender or involved side at the 6-month follow-up ($p > 0.05$).

The primary predictor variables against secondary outcome variables are listed in Tables 7 and 8. At the end of the treatment in group I, maximum pain at rest, chewing efficiency, and quality of life values for both treatment groups showed significant improvements compared to the baseline values ($p < 0.05$). MNMO, MAMO, and TMJ sound values showed significant improvements only in group Ib. None of the outcome variables in the control group had changed at the 6-month follow-up ($p > 0.05$). When comparing the secondary variables between groups at the end of the treatment, MNMO, MAMO, chewing efficiency, and quality of life values were significantly higher in both treatment groups than control group ($p < 0.05$). However, improvements in quality of life and chewing efficiency values were significantly better in group Ib than group Ia. At the end of treatment, the TMJ sounds value of group Ib was slightly lower than that of group Ia, but the difference was not significant ($p = 0.543$). The treatment effectiveness value of group Ib was slightly higher than that of group Ia, but the difference was not significant ($p = 0.06$).

Table 1
Descriptive statistics of the group I (N = 45 patients, 58 TMJs) and study variables.

Variable	Group Ia	Group Ib	Group Ic	*P*
	HA Injection	AC + HA	Control	
	(n = 18 patients)	(n = 18 patients)	(n = 9 patients)	
Age (years)				
Mean ± SD	31.67 ± 13.53	29.78 ± 12.95	29.67 ± 13.70	0.894
Range	(16–56)	(16–62)	(19–62)	
Gender, n (%)				
Men	1 (5.6)	2 (11.1)	1 (11.1)	0.434
Women	17 (94.4)	16 (88.9)	8 (88.9)	
Involved side, n (%)				
Right	7 (38.9)	5 (27.8)	3 (33.3)	0.372
Left	6 (33.3)	9 (50.0)	2 (22.2)	
Bilateral	5 (27.8)	4 (22.2)	4 (44.4)	
Duration of symptoms, n (%)				
6–12 months	12 (52.2)	14 (63.7)	5 (38.5)	0.355
> 12 months	11 (47.8)	8 (36.3)	8 (61.5)	
Total TMJs (n)	23	22	13	

Data are presented as mean ± standard deviation or number (percentage); n, number; SD, standard deviation; TMJ, temporomandibular joint; HA, hyaluronic acid; AC, arthrocentesis.

Table 2
Descriptive statistics of the group II (N = 45 patients, 58 TMJs) and study variables.

Variable	Group IIa	Group IIb	Group IIc	*P*
	HA injection	AC + HA	Control	
	(n = 19 patients)	(n = 18 patients)	(n = 8 patients)	
Age (years)				
Mean ± SD	31.05 ± 15.91	40 ± 12.74	46.38 ± 21.62	0.59
Range	(15–61)	(18–67)	(21–82)	
Gender, n (%)				
Men	3 (15.8)	2 (11.1)	3 (37.5)	0.353
Women	16 (84.2)	16 (88.9)	5 (62.5)	
Involved side, n (%)				
Right	7 (36.8)	5 (27.8)	4 (50.0)	0.969
Left	8 (42.1)	6 (33.3)	2 (25.0)	
Bilateral	4 (21.1)	7 (38.9)	2 (25.0)	
Duration of symptoms, n (%)				
6–12 months	11 (47.8)	16 (64.0)	2 (20.0)	0.064
> 12 months	12 (52.2)	9 (36.0)	8 (80.0)	
Total TMJs (n)	23	25	10	

Data are presented as mean ± standard deviation or number (percentage); n, number; SD, standard deviation; TMJ, temporomandibular joint; HA, hyaluronic acid; AC, arthrocentesis.

Table 3
Comparison between individual study variables and primary outcome variables 6 months after treatment.

Variable	Group I (DDwR)		Grup II (DDwoR)	
	Pain on chewing (VAS)	*P*	Pain on chewing (VAS)	*P*
Gender, n (%)				
Men	3.00 (0–9)	0.344	3.00 (0–7)	0.527
Women	3.00 (0–7)		3.00 (0–9)	
Involved side, n (%)				
Right	3.00 (0–9)	0.847	3.00 (0–9)	0.857
Left	3.00 (0–7)		3.00 (0–7)	
Bilateral	2.00 (0–7)		2.00 (0–7)	
Duration of symptoms, n (%)				
6–12 months	2.00 (0–8)*	0.002*	2.00 (0–9)#	0.001#
>12 months	3.00 (0–8)*		4.00 (0–9)#	

Data presented as median (minimum–maximum); VAS, visual analog scale; DDwR, disc displacement with reduction; DDwoR, disc displacement without reduction; n, number.
*,# Statistically significant as indicated in *P* values.

Table 4
Comparison between primary predictor variables and primary outcome variables in group I.

	Time	Group Ia	Group Ib	Group Ic	*P*
		(HA; n = 23)	(AC + HA; n = 22)	(Control; n = 13)	
Pain on chewing (VAS)	Preop	6.00 (3–10)	7.00 (3–10)	5.00 (2–8)	0.104
	6 months	4.00 (0–8)*	2.00 (0–7)#	5.00 (2–8)*,#	0.006*; <0.001#
P		<0.001	<0.001	0.414	

Data presented as median (minimum–maximum); VAS, visual analog scale; HA, hyaluronic acid; AC, arthrocentesis; n, number.
*,# Statistically significant as indicated in *P* values.

Table 5
Comparison between primary predictor variables and primary outcome variables in group II.

	Time	Group IIa	Group IIb	Group IIc	*P*
		(HA; n = 23)	(AC + HA; n = 25)	(Control; n = 10)	
Pain on chewing (VAS)	Preop	7.00 (3–10)	8.00 (2–10)	5.00 (1–8)	0.134
	6 months	4.00 (0–6)*	2.00 (0–9)#	5.50 (4–7)*,#	0.004*; 0.001#
P		<0.001	<0.001	0.476	

Data presented as median (minimum–maximum); VAS, visual analog scale; HA, hyaluronic acid; AC, arthrocentesis; n, number.
*,# Statistically significant as indicated by *P* values.

In group II, MNMO, MAMO, maximum pain at rest, chewing efficiency, and quality of life values in the treatment groups showed significant improvements as compared to the retrospective baseline values at the end of the treatment ($p < 0.05$). None of the outcome variables in the control group had significantly changed at the 6-month follow-up ($p > 0.05$). There was an increase in TMJ sound score in group IIb, but this was not statically significant. When comparing the secondary variables among

Table 6
Comparison between individual study variables and secondary outcome variables 6 months after treatment.

	Variable	MNMO	MAMO	Max pain at rest	Chewing efficiency	TMJ noise	Treatment tolerability	Treatment effectiveness	Quality of Life
Group I (DDwR)	*Gender*								
	Men	44.50 (28–47)	47.50 (34–50)	0 (0–2)	7 (5–8)	0.50 (0–1)	2 (1–3)	3 (2–3)	70 (23–90)
	Women	40 (26–50)	42 (28–53)	0 (0–5)	7 (2–10)	1 (0–2)	2 (0–4)	3 (1–4)	57.5 (33–75)
	P	0.107	0.059	0.082	0.533	0.944	0.124	0.791	0.530
	Involved side								
	Right	40 (27–50)	42.00 (32–50)	0 (0–2)	8 (2–10)	0 (0–1)	2 (1–4)	2.50 (2–4)	71.00 (30–85)
	Left	40 (31–50)	42.00 (35–53)	0 (0–5)	7 (2–10)	1 (0–2)	2 (1–3)	3.00 (1–4)	70.00 (40–90)
	Bilateral	38 (26–45)	43.00 (28–48)	0 (0–2)	7 (3–9)	1 (0–2)	1 (0–3)	3.00 (1–3)	37.50 (23–78)
	P	0.436	0.606	0.502	0.652	0.063	0.968	0.949	0,06
	Duration of symptoms								
	6–12 months	40 (28–50)	42.00 (34–53)	0 (0–3)	7 (4–10)*	1 (0–2)	2 (1–4)	3.00 (0–4)†	75.00 (35–90)#
	>12 months	38.00 (26–47)	42.00 (28–50)	1 (0–4)	6 (1–8)*	1 (0–2)	2 (0–3)	2.00 (0–3)†	45.00 (20–85)#
	P	0.166	0.128	0.274	<0.001*	0.360	0.275	<0.001†	<0.001#
Group II (DDwoR)	*Gender*								
	Men	35 (25–45)	36 (26–48)	0 (0–2)	7 (1–10)	0 (0–1)	3 (2–4)	2 (1–4)	65 (23–90)
	Women	32.50 (22–50)	35 (26–50)	0 (0–3)	5 (3–8)	0 (0–1)	2 (0–4)	2 (0–4)	42.5 (10–80)
	P	0.624	0.437	0.255	0.277	0.971	0.079	0.964	0.717
	Involved side								
	Right	35.00 (25–50)	36.00 (26–50)	0 (0–2)	7.5 (3–10)	0 (0–1)	2 (1–4)	2.50 (1–4)	52.50 (10–90)
	Left	31.50 (22–42)	33.00 (26–45)	0 (0–2)	6.5 (1–10)	0 (0–1)	1.5 (0–4)	2.00 (0–4)	62.50 (25–85)
	Bilateral	35 (25–42)	38 (26–43)	0 (0–3)	7 (3–9)	0 (0–1)	2 (1–4)	3 (0–4)	67.5 (23–90)
	P	0.621	0.649	0.186	0.195	0.067	0.437	0.833	0.173
	Duration of symptoms								
	6–12 months	35.00 (25–42)	38.00 (29–44)†	0 (0–3)	8.0 (1–10)*	1 (0–2)	2 (1–4)	3.00 (1–4)¶	75.00 (30–90)#
	>12 months	30.00 (22–45)	31.00 (26–48)†	1 (0–3)	5 (1–10)*	0 (0–1)	2 (0–4)	2.00 (0–4)¶	45.00 (10–75)#
	P	0.093	0.034†	0.246	0.001*	0.055	0.141	0.002¶	<0.001#

Data are presented as median (minimum–maximum). MNMO, maximum non-assisted mouth opening; MAMO, maximum assisted mouth opening; TMJ, temporomandibular joint, DDwR; disc displacement with reduction; DDwoR; disc displacement without reduction.
*, †, #, ¶ Statistically significant as indicated by *P* values.

Table 7
Comparison between primary predictor variables and secondary outcome variables in group I.

	Time	Group Ia (HA; n = 23)	Group Ib (AC + HA; n = 22)	Group Ic (Control; n = 13)	*P*
MNMO	Preop	37.00 (26–50)	37.50 (26–46)	36.00 (26–41)	0.611
	6 months	40.00 (26–50)*	42.00 (34–50)#	32.00 (27–41)*,#	0.034*; 0.001#
P		0.879	<0.001	0.481	
MAMO	Preop	40.00 (29–50)	39.50 (26–47)	40.00 (31–43)	0.513
	6 months	43.00 (28–53)*	44.00 (35–50)#	38.00 (32–45)*,#	0.026*; 0.008#
P		0.434	<0.001	0.959	
Max pain at rest, VAS	Preop	1.00 (0–7)	2.00 (0–5)	1.00 (0–5)	0.558
	6 months	0.00 (0–4)	0.00 (0–4)	1.00 (0–3)	0.079
P		0.002	0.001	0.414	
Chewing efficiency	Preop	4.00 (2–7)	4.00 (2–7)	4.00 (1–6)	0.973
	6 months	7.00 (2–10)*,¶	8.00 (3–9)#,¶	5.00 (1–7)*,#	<0.001#; 0.016*; 0.041¶
P		<0.001	<0.001	0.070	
TMJ noise	Preop	1.00 (0–2)	1.00 (0–2)	1.00 (0–2)	0.310
	6 months	1.00 (0–2)	0.00 (0–2)	1.00 (0–2)	0.897
P		0.660	0.003	0.317	
Quality of life	Preop	45.00 (20–55)	45.00 (30–65)	50 (35–60)	0.615
	6 months	55.00 (20–90)*,¶	75.00 (35–90)#,¶	45 (20–65)*,#	<0.001#; 0.047*; 0.021¶
P		0.003	<0.001	0.161	
Treatment Tolerability	6 months	2.00 (0–3)	2.00 (1–4)		0.744
Treatment effectiveness	6 months	2.00 (0–4)	3.00 (1–4)		0.06

Data are presented as median (minimum–maximum); MNMO, maximum non-assisted mouth opening; MAMO, maximum assisted mouth opening; TMJ, temporomandibular joint; HA, hyaluronic acid; AC, arthrocentesis; n, number.
*,#,¶ Statistically significant as indicated by *P* values.

groups, MNMO, MAMO, chewing efficiency, and quality of life values at the end of the treatment were significantly higher in all treatment groups than in the control group ($p < 0.05$); however, the improved quality of life scores were significantly higher in group IIb than group IIa ($p = 0.004$). The values of TMJ sound of group IIa were slightly lower than that of group IIb, but the difference was not significant ($p > 0.05$). The treatment tolerability scores of group IIa were significantly lower than group IIb ($p = 0.04$). The treatment effectiveness value of group IIb was slightly better than that of group IIa, but the difference was not significant ($p = 0.059$).

4. Discussion

Although HA injection and arthrocentesis plus HA injection are widely used in the treatment of DDwR and DDwoR, the available literature has not yielded any definitive conclusion on the most suitable treatment protocol (Manfredini et al., 2012; Korkmaz et al.,

Table 8
Comparison between primary predictor variables and secondary outcome variables in group II.

	Time	Group IIa (HA; n = 23)	Group IIb (AC + HA; n = 25)	Group IIc (Control; n = 10)	*P*
MNMO	Preop	27.00 (18–41)	26.00 (18–48)	26.00 (22–42)	0.990
	6 months	32.00 (25–45)*	36.00 (26–42)#	26.50 (22–37) *,#	0.018*; 0.004#
P		<0.001	<0.001	0.904	
MAMO	Preop	27.00 (21–46)	30.00 (18–38)	27.00 (24–43)	0.965
	6 months	35.00 (28–48)*	38.00 (26–44)#	29.00 (26–39)*,#	0.004*; 0.002#
P		<0.001	<0.001	0.778	
Max pain at rest, VAS	Preop	1.00 (0–6)	2.00 (0–8)	1.00 (0–3)	0.064
	6 months	0.00 (0–2)	0.00 (0–3)	1.50 (0–3)	0.134
P		0.001	<0.001	0.257	
Chewing efficiency	Preop	3.00 (0–6)	4.00 (1–7)	3.50 (1–7)	0.411
	6 months	6.00 (3–10)*	8.00 (1–10)#	3.50 (1–5)*,#	0.001*; <0.001#
P		<0.001	<0.001	0.516	
TMJ noise	Preop	0.00 (0–2)	0.00 (0–2)	0.00 (0–2)	0.255
	6 months	0.00 (0–2)	1.00 (0–2)	0.00 (0–2)	0.070
P		0.132	0.984	0.317	
Quality of life	Preop	40.00 (10–55)	35.00 (10–50)	37.50 (25–55)	0.982
	6 months	60.00 (30–80) *,¶	80.00 (10–90)#,¶	40.00 (20–50)*,#	<0.001*,#; 0.004¶
P		<0.001	<0.001	0.986	
Treatment tolerability	6 months	3.00 (1–4)*	1.00 (0–3)*		0.04*
Treatment effectiveness	6 months	2.00 (1–3)	3.00 (0–4)		0.059

Data are presented as median (minimum–maximum); MNMO, maximum non-assisted mouth opening; MAMO, maximum assisted mouth opening; TMJ, temporomandibular joint; HA, hyaluronic acid; AC, arthrocentesis; n, number.
*,#,¶ Statistically significant as indicated by *P* values.

2016). In this study, we compared the commonly used treatment protocols, and evaluated which treatment method is more effective for TMJ DDwR and DDwoR.

Epidemiological studies have documented that TMJ disorders are more frequent in females than males. Although hormonal, psychosocial, and genetic factors are mentioned as reasons, no definite conclusion has been drawn (Bagis et al., 2012; Chisnoiu et al., 2015). Similarly, the prevalence of female patients was higher in our study. TMJ disorders are seen most commonly between 20 and 40 years of age (Manfredini et al., 2006). The majority of patients were between the 2nd and 4th decades (83%) in our study, and the mean age was 33.9 years.

Patients usually need treatment to reduce pain in jaw functions. When evaluating a treatment approach, one of the most important parameters is the decrease or elimination of pain (Bagis et al., 2012; Tuncel, 2012). Inflammation of the synovial fluid, capsule or retrodiscal tissues and increased intracapsular pressure and presence of fibrous adhesions cause pain (Neeli et al., 2010; Sipahi et al., 2015). Comparative studies have reported that arthrocentesis effectively relieves the pain in symptomatic joints (Carvajal and Laskin, 2000; Guarda-Nardini et al., 2010). Removal of pain is achieved by some effects of arthrocentesis, such as removal of inflammatory cells from the synovial fluid, elimination of adhesions, and provision of natural intra-articular pressure (Neeli et al., 2010; Sharma et al., 2013). HA, corticosteroids, morphine, and tenoxicam injections can be administered with arthrocentesis to increase the effectiveness of the treatment (Manfredini et al., 2012; Sipahi et al., 2015). HA injection following arthrocentesis was first performed by Kopp et al. (1985) as an alternative to corticosteroids. They reported that HA could be a good alternative because of the successful results and no known side effects (Kopp et al., 1985). The present study showed that arthrocentesis plus HA injection improved the maximum pain on chewing values at the 6-month follow-up. The maximum pain on chewing value decreased markedly from 7 to 2 for group Ib, and from 8 to 2 for group IIb. These outcomes were compatible with data in the literature and support the efficacy of arthrocentesis plus HA injection for DDwR and DDwoR treatments.

Sodium hyaluronate, which is produced by the synovial membrane and forms a large part of the synovial fluid, plays an important role in joint lubrication, protecting joint cartilage, and nourishing joint avascular structures (Yeung et al., 2006; Basterzi et al., 2009). Inflammation in the TMJ reduces the molecular weight and concentration of HA, thereby reducing the physiological effects of synovial fluid, such as shock absorption and lubrication (Kawai et al., 2004; Guarda-Nardini et al., 2007). Intra-articular HA injection has successfully been used in the pain control of TMJ disorders due to their anti-inflammatory and analgesic effects, such as scavenging for free radicals, reducing vascular permeability, and inhibition of phagocytosis, chemotaxis, prostaglandin synthesis, metalloproteinase activity (Tuncel, 2012; Korkmaz et al., 2016). The present study showed that single HA injection reduced the pain on chewing values at 6-month follow-up in groups Ia and IIa. The maximum pain on chewing value decreased markedly from 6 to 4 in group Ia and from 7 to 4 in group IIa.

The maximum pain at rest is not commonly evaluated in the literature. Sharma et al. (2013) and Guarda-Nardini et al. (2012) reported that arthrocentesis plus HA injection reduced the pain at rest values in patients with TMJ internal disorders. In this study, there was no significant difference between control and treatment groups in maximum pain at rest values at the end of the 6-month follow-up. Presumably, these values were within low ranges at the baseline.

Another important problem is the limitation of mouth opening in TMJ disorders. This limitation negatively affects chewing function and quality of life (Chisnoiu et al., 2015). Arthrocentesis increases disc mobilization and removes adhesions, thus making joint movements easier (Guarda-Nardini et al., 2010; Tozoglu et al., 2011). HA injection provides lubrication that reduces friction of the joint surfaces, thus increasing movement capacity of the joint (Yeung et al., 2006). Relief of pain and a decrease in the negative pressure also improve mouth opening (Korkmaz et al., 2016). Similar to previous studies, MAMO and MNMO values increased in all treatment groups at the 6-month follow-up when compared to the baseline values in our study.

Evaluation of chewing efficiency and quality of life is an important outcome for the measurement of the treatment success

(Guarda-Nardini et al., 2007; Korkmaz et al., 2016). In the present investigation, these values markedly increased after treatments. This could be explained by the improvements in the clinical symptoms of the patients (Guarda-Nardini et al., 2007; Korkmaz et al., 2016). Chewing efficacy and quality of life values in arthrocentesis plus HA groups were higher than HA injection groups at the 6-month follow-up. This may be due to higher improvements in clinical parameters of the arthrocentesis plus HA treated groups.

Some patients state that joint sounds cause problems in their social life. The difference in joint sounds after treatments is controversial. Sharma et al. (2013) reported that arthrocentesis decreased joint sounds in TMJ internal derangement. One study reported that joint noises increased after arthrocentesis in DDwR and did not change in DDwoR (Carvajal and Laskin, 2000). It is stated that after intra-articular HA injection, joint sounds may decrease; however, some investigators reported that these treatments do not markedly improve joint sounds (Hepguler et al., 2002; Sato et al., 2003). In our study, significant reduction in joint sounds was observed only in group Ib, and no significant difference was seen between the treatment and control groups at the end of the follow-up period. There was an increase in TMJ noise in group IIb. This was possibly caused by improved disc mobility after lysis and lavage. When treatment for internal derangement is initiated, reduction of pain is an essential goal. However, whether cessation of TMJ sounds should be a therapeutic goal is controversial (Sato et al., 2003).

Assessment of treatment tolerability is important for patients with high anxiety. Failure to cooperate with these patients during treatment may reduce the success. Guarda-Nardini et al. (2007) assessed treatment tolerability in patients undergoing arthrocentesis plus HA injection, and the mean score was 2.36 ± 0.99. In another study, mean treatment tolerability value was 2.40 in patients treated with HA injection (Guarda-Nardini et al., 2014). In this study, treatment tolerability value was lower in group IIb. This was probably due to the high pain values at baseline in group IIb and the fact that DDwoR is a more painful condition. General anesthesia may be preferred when treatments cannot be performed effectively under local anesthesia.

Subjective evaluation of treatment effectiveness is important to measure the success and reliability of treatment. Patients evaluated the efficacy of arthrocentesis in one study and 84% of them rated the treatment as ‘good’ or ‘excellent’ (Guarda-Nardini et al., 2007). In another study, mean treatment effectiveness value was 2.40 in patients treated with HA injection (Guarda-Nardini et al., 2014). In the present study, treatment effectiveness value was 2.00 in group Ia and IIa, and 3.00 in group Ib and IIb. This is primarily because the clinical parameters are better in arthrocentesis plus HA groups than single HA groups.

The success of treatments for TMJ disorders can be influenced by many factors, such as age, oral habits or time of onset (Kaneyama et al., 2007; Kim et al., 2014). Aktas et al. (2010) reported that duration of locking and degenerative changes were the significant factors that influenced treatment outcomes in patients with DDwoR. Murakami et al. (1995) stated that form and adaptability of the disc and the posterior band might be better preserved when the duration of locking is short. In this study, some clinical parameters in group I and group II were affected by the duration of symptoms. When the duration of the symptoms was >12 months, these values were found to be significantly lower. According to our results, treatment should be started early, because adaptive capacity of articular structures decreases over time and destruction increases.

Untreated disc displacements can result in spontaneous remission, development of adaptive changes, and progression of irregularity, or remain unchanged (Sato et al., 1997a, 1997b; Zhang et al., 2009). One study reported that in patients with DDwR not undergoing treatment, the range of mandibular movement, reciprocal clicking, and TMJ pain remain unchanged over time, but masticatory muscle tenderness tended to lessen (Sato et al., 2003). Conversely, some studies reported that the DDwR might convert to DDwoR, and internal derangements are likely to progress to osteoarthritis (Stegenga, 2001; Sato et al., 2003). Many studies have reported that treated patients exhibited better outcomes than untreated patients. Similarly, clinical improvements in treatment groups were better than control groups in this study, and none of the outcomes differed at the 6-month follow-up for the control groups.

The results of this study showed that arthrocentesis plus HA injection and single HA injection decreased the maximum pain at rest and maximum pain on chewing, increased MNMO and MAMO, and improved quality of life and chewing efficiency in patients with DDwR or DDwoR. Additionally, arthrocentesis plus HA injection was more effective in improving pain, chewing efficiency, quality of life, and maximum mouth opening than single HA injection. These results are consistent with those of Xinmin and Jian (2005), who reported that arthrocentesis plus HA injection was more effective than single HA injection or arthrocentesis. No clinical improvements were observed in control groups during follow-up.

The limitation of this study was the low number of patients and short follow-up period. The effectiveness of arthrocentesis plus HA injection and single HA injection could change in long follow-up periods. Nitzan et al. (1997) suggested that the healing process took a long time in patients older than 40 years of age. Additionally, it would be useful to include more variables that affect treatment outcomes, such as varied age ranges, preoperative degree of pain, and parafunctional habits. Murakami et al. (1995) reported that the mean patient age of failed cases was higher than that of the successful cases. One study reported that severe preoperative pain may be a predictor of the effectiveness of arthrocentesis (Nishimura et al., 2001).

5. Conclusion

Arthrocentesis plus HA injection and single HA injection effectively alleviated the signs and symptoms of patients with painful TMJ DDwR or DDwoR except for TMJ sounds. According to our results, arthrocentesis plus HA injection showed much better outcomes than single HA injection for chewing efficiency and quality of life in patients with DDwR and quality of life in patients with DDwoR. We recommend performing the combination of arthrocentesis and HA injection in treatment of TMJ DDwR or DDwoR. Spontaneous resolution of clinical signs and symptoms was not seen in untreated patients, therefore, administration of treatment procedures in TMJ internal derangements would be rational. The duration of symptoms is related to the outcomes, so treatment should be initiated without delay. These findings need to be confirmed by future researches with an appropriate design to overcome the present study's limitations.

Funding source

There was no funding source for this work.

Authors' contributions

OY and YTK designed the study and performed treatments. OY, YTK, and TT collected and analysed data, and wrote the manuscript. All authors read and approved the final version of the manuscript.

Conflicts of interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2019.07.030.

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