Does Arthrocentesis Reduce Pain in Patients With Systemic Polyarthritis and Temporomandibular Joint Intra-Articular Pain and Dysfunction?

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Background: Arthrocentesis is effective at reducing pain and improving function in patients with temporomandibular joint intra-articular pain and dysfunction (IPD). It remains unclear if it is equally effective in patients with systemic polyarthritis (SPA) and IPD.

Purpose: The purpose of this study was to compare changes in pain and function following arthrocentesis for IPD in subjects with and without SPA.

Study Design, Setting, Sample: This retrospective cohort study was conducted on patients diagnosed with IPD, treated with a cycle of 3 arthrocentesis plus hyaluronic acid at the Hospital of Treviso, Italy, between 2022 and 2023. Inclusion criteria were adult patients with or without SPA with IPD unresponsive to first-line treatments. Patients with other systemic diseases, a history of temporomandibular joint surgery, and head/neck trauma were excluded.

Predictor Variable: The primary predictor variable was presence of SPA (yes/no).

Main Outcome Variable(s): Primary outcome variable was therapeutic effect measured as change in masticatory efficiency, maximum pain at chewing, and maximum pain at rest between T0 (before treatment) and T1 (3 months after treatment). Secondary outcomes were change in range of motion and self-reported functional limitation between T0 and T1.

Covariates: Covariates included demographics (age, sex) and surgery (bilateral arthrocentesis).

Analyses: Mann-Whitney *U* test was adopted for single variable analysis of covariates, primary outcome variables, and secondary outcome variables compared to predictor variable (SPA). Spearman correlation test was used to assess the influence of covariates on primary outcome variable. Statistical significance was set at $P < .05$.

Results: Final sample size included 58 subjects, with 29 subjects in each group. Mean age (SD) for IPD with SPA and IPD without SPA groups was 53.5 ($\pm$17.6) and 54.9 ($\pm$15.6) ($P = .7$), respectively. Each group contained the same number of males (n = 2) and females (n = 27) ($P = .9$). No significant differences were found between groups in change of masticatory efficiency (SPA: 45.49 $\pm$ 76.56; non-SPA: 38.45 $\pm$ 55.68; $P = .8$), maximum pain at chewing (SPA: -69.14 ± 35.36; non-SPA: -49.64 ± 45.16; $P = .6$), or maximum pain at rest (SPA: -53.14 ± 46.97; non-SPA: -35.81 ± 90.34; $P = .9$).

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Conclusion and Relevance: Arthrocentesis with hyaluronic acid appears to be equally effective in subjects with IPD irrespective of the presence of SPA.

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Temporomandibular disorders (TMDs) is an umbrella term for a heterogeneous group of musculoskeletal conditions that affect the temporomandibular joint (TMJ), the jaw muscles, and/or the associated structures, typically presenting with symptoms such as pain, functional limitation, and joint noises.[1] This term actually encompasses distinct conditions that, although potentially coexisting in the same patient, can have different clinical presentations, etiological factors, and treatment approaches.[2] Recent studies have highlighted that when the source of the problem lies within the TMJ, the use of the term "intra-articular pain and dysfunction" (IPD) is clinically and pathophysiologically recommendable.[3,4]

Conditions affecting the TMJ are quite prevalent in the general population, impacting approximately 31% of adults and 11% of children.[5] The etiology of IPD is multifactorial; the biopsychosocial model is the current paradigm that best explains the onset of jaw and facial pain.[4,6] A combination of mechanical overload in the form of awake and sleep bruxism together with predisposing psychological factors (eg, anxiety, depression) and comorbid medical and sleep-related disorders seems to contribute to the presence and persistence of IPD signs and symptoms.[7-15] The whole scenario is further complicated by the difficulties that patients often encounter in finding appropriate care.[16] IPD can also be more prevalent in specific populations, such as in patients with systemic diseases; in particular, the TMJ may be more prone to develop painful symptoms in patients affected by rheumatic diseases, such as rheumatoid arthritis.[17,18]

Rheumatic diseases are a group of immune-mediated disorders (autoimmune or inflammatory) characterized by a chronic inflammatory condition, typically affecting the body with a multi-organ pattern.[19] Musculoskeletal and connective tissues are the most commonly impacted; however, the immune system can target not only joints, tendons, and muscles but also internal organs. Currently, more than 100 rheumatic diseases have been classified, each with a different etiology and clinical presentation.[19] Within this wide spectrum of conditions, systemic polyarthritis (SPA) encompasses all the rheumatological conditions that affect 5 or more joints.[20] Examples of SPA include rheumatoid arthritis, psoriatic arthritis, and adult-onset Still's disease.[20] The prevalence of TMJ IPD in rheumatic patients is highly variable, depending on the type of disease, the population studied, and the diagnostic classification system; nevertheless, compared to the general population, individuals affected by rheumatic diseases seem to have a higher prevalence of TMJ impairment. Several studies have indeed shown that both SPA and one of its most common subtypes, rheumatoid arthritis, are significant risk factors for TMJ pain.[21-23] However, in the literature, there are no reported studies on the management of IPD in patients with SPA.

Based on standard of care recommendations, IPD management should always start with noninvasive therapies primarily based on cognitive behavioral therapy, anti-inflammatory drugs, physical therapy, and oral appliances.[1,4,24] Cases nonresponsive to such treatments can benefit from an intervention with arthrocentesis.[3,4,24,25] TMJ arthrocentesis represents a second-line treatment and consists of lavage of the joint space through saline or Ringer lactate solution, in combination with the positioning of various medication substances (eg, hyaluronic acid [HA], corticosteroids, platelet-rich plasma, and human amniotic membrane) for the purpose of removing inflammatory byproducts.[26-28]

Although the lavage has been shown to be helpful in many systemic joint pathologies, clinical trials on TMJ arthrocentesis then exclude patients with rheumatic disorders to avoid possible confounding factors.[29-35] A study performed by Trieger et al in 1999 showed in a population of 22 females affected by rheumatoid arthritis, that arthrocentesis can have a positive effect on pain.[30] Despite this, the lack of a control group and the small sample size of the study make it difficult to draw clinically relevant conclusions. In the current state of evidence, there is a lack of research on the outcome of arthrocentesis in patients affected by rheumatic disorders, such as SPA. Little is known if systemic impairment has an influence on the functional recovery of the stomatognathic system following treatment with arthrocentesis. The complexity of articular pathology is undoubtedly different in patients affected by SPA; therefore, it could be hypothesized that SPA patients could have a reduced repair potential of TMJ due to the underlying systemic condition.

Within these premises, the purpose of the present investigation was to compare changes in pain and

function following arthrocentesis for IPD in subjects with and without SPA. The null hypothesis was that there was no significant difference between patients with and without SPA regarding the clinical effects of arthrocentesis. The first aim of this study was to compare the therapeutic effect, measured as change in masticatory efficiency, between the SPA group and the non-SPA group at a 3-month follow-up, following the treatment with 3 cycles of arthrocentesis plus HA supplementation. The second aim was to assess the change in maximum pain at rest between the 2 groups. The third aim was to assess the change in maximum pain at chewing. Finally, the fourth aim was to measure the change in mandibular functional outcomes (measured as change in range of motion and functional limitation perceived).

Material and Methods

STUDY DESIGN/INCLUSION/EXCLUSION CRITERIA

The researchers implemented a retrospective cohort study. Subjects presenting to the Unit of Oral and Maxillofacial Surgery of Ca'Foncello Hospital (Treviso, Italy) with IPD between June 2022 and November 2023 who underwent arthrocentesis and HA injections were identified from a review of the electronic medical records. The inclusion criteria included adults from 18 to 80 years, diagnosis of IPD based on diagnostic criteria/TMD history and examination, and failure to improve following nonsurgical treatment (counseling, cognitive-based therapy, and physical therapy).[36] Patients who had previously undergone surgical interventions on the TMJs and those with a history of head or neck trauma were excluded from the study. Additionally, patients with any other concomitant systemic disease (eg, cardiovascular, metabolic disorders, etc) were also excluded.

Both electronic health records and paper medical records were reviewed for demographics and operative variables for study subjects. All participants signed an informed consent form to use their records for this study, which was approved by the institutional review board of the Ca'Foncello Hospital, Treviso, with the number "581/CE Marca." All individuals gave their informed consent to the interventions, in accordance with the Declaration of Helsinki, and understood that they were free to withdraw from the study at any time.

PREDICTOR VARIABLE

The predictor variable was the presence/absence of the rheumatic disease (SPA) in a clinical context of concomitant IPD, according to which patients were divided into 2 groups.

OUTCOME VARIABLES

The primary outcome variable was therapeutic effect, measured as the change before and after the treatment in the following parameters:

- Maximum pain at chewing and at rest, which were assessed by a visual analog scale from 0 to 10, with 0 representing no pain and 10 representing the worst pain ever experienced
- Masticatory efficiency, evaluated by a visual analog scale from 0 to 10, with 0 representing the capability to eat only soft food and 10 representing the possibility to eat also the hardest food without any problem.

The secondary variable was mandibular functional outcomes, as was measured by the change before and after the treatment in the following parameters:

- Maximum nonassisted opening, estimated in millimeters;
- Maximum assisted opening, estimated in millimeters;
- Functional limitation perceived by the patient, evaluated by a Likert-type scale with 0 as the worst outcome and 4 as the best (ie, absence of limitation).

The outcome variables were evaluated according to the methods proposed in previous studies on TMJ arthrocentesis.[37-39] For each patient, primary and secondary variables were assessed preoperatively, right before the first arthrocentesis (T0). Moreover, all the measurements were reassessed after the end of the treatment at a 3-month follow-up (T1). All the outcomes were measured at the patient level.

COVARIATES

The covariates were demographics (age, sex) and surgical (bilateral arthrocentesis).

PROCEDURE

All patients underwent an arthrocentesis procedure based on the single-needle technique performed by 2 oral and maxillofacial surgeons (M.V. and L.G. N.).[40] After disinfecting the skin in the preauricular area, 2 local anesthesia injections are performed in the tissues surrounding the TMJ (Fig 1) and inside the TMJ capsule (Fig 2), respectively. The first anesthesia is achieved with 1 ml of mepivacaine 2% with vasoconstrictor, while the intracapsular one is performed using 2 ml of mepivacaine 2% without vasoconstrictor. Once good pain control has been obtained, the Holmlund line is used as a reference

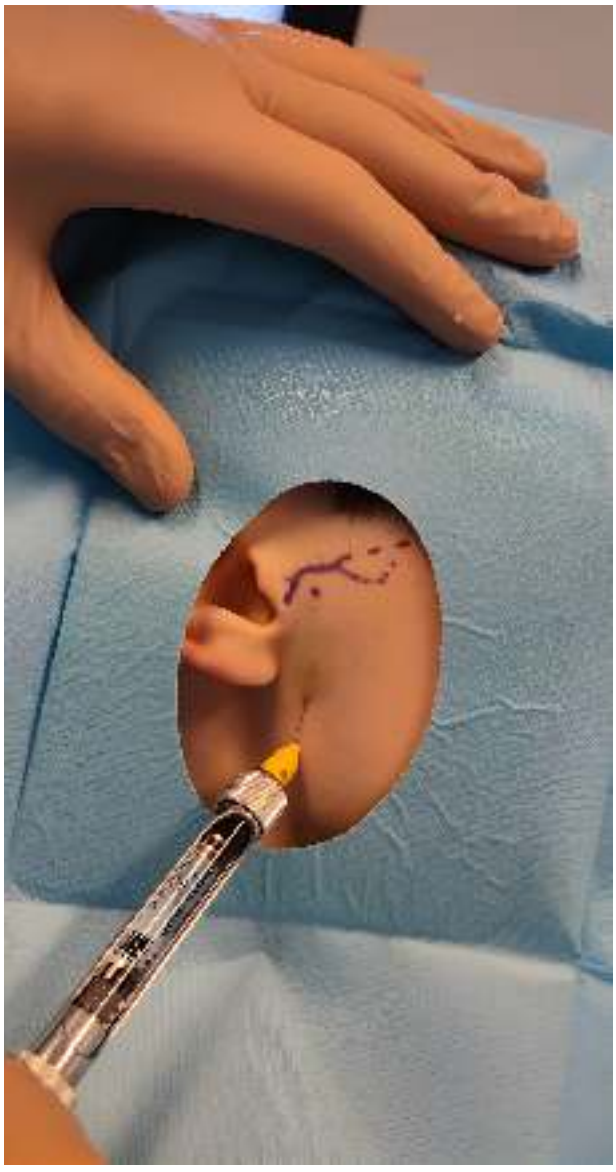

FIGURE 1. Anesthesia in the tissues surrounding the temporomandibular joint.

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point to locate the TMJ glenoid fossa (Fig 3). An 18 G needle is inserted about 10 mm in front of the tragus and 2 mm under the line with the patient in an open-mouth position (Fig 4). While the subject remains with the open mouth, 1-2 ml of saline solution is introduced through the needle (Fig 5). The patient then closes the mouth, and the fluid introduced in the joint flows out through the same needle used for the injection of the saline solution (Fig 6). The procedure is repeated until the amount of 10-50 ml of saline is reached. Subsequently, the needle is used to deliver 1 ml of medium molecular weight HA (Synovial 16 mg/2 ml, IBSA Farmaceutici, Lodi, Italy) (Fig 7).

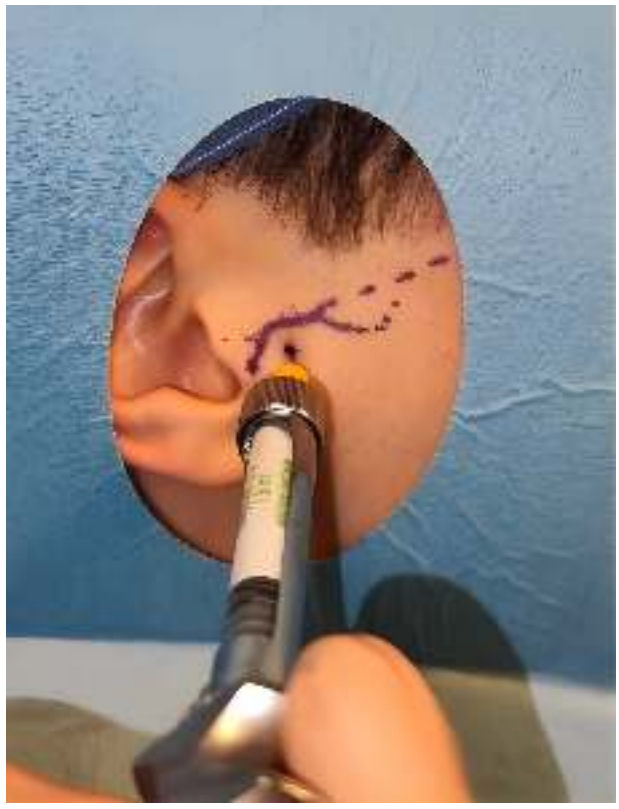

FIGURE 2. Intracapsular anesthesia.

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FIGURE 3. The Holmlund line from the lateral cantus to the tragus.

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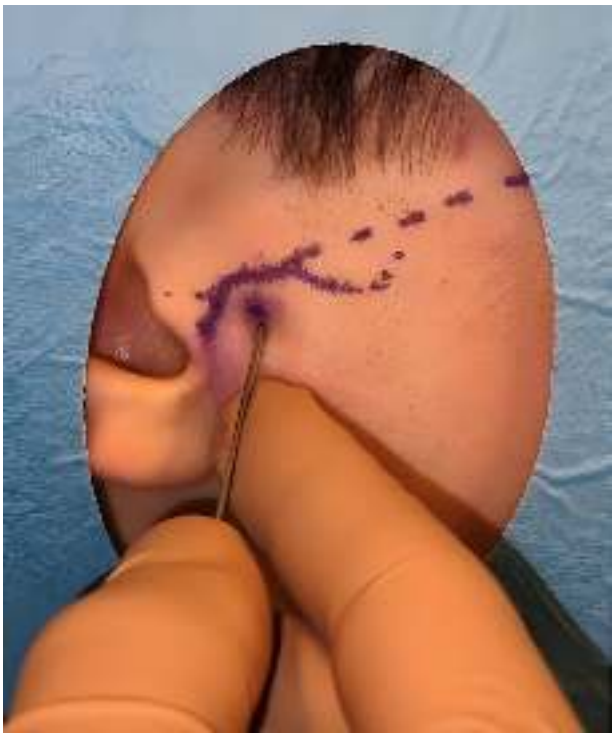

FIGURE 4. Needle insertion 10 mm after and 2 mm below the tragus.

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FIGURE 5. Introduction into the temporomandibular joint of saline solution through the needle.

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For each patient, the procedure was repeated every 2 weeks for a total of 3 procedures.

DATA COLLECTION METHOD

Based on sample size calculation and power analysis, 2 groups of patients with TMJ IPD (with or without the presence of SPA) were selected. At first, a group of patients with TMJ IPD and concomitant SPA was randomly selected from the hospital database using Excel Software (Los Angeles, California, USA). The group of patients with TMJ IPD without SPA was instead randomly selected from the hospital database, requiring them to have the same gender distribution, the same number of patients that underwent bilateral or unilateral arthrocentesis, and no significant difference in mean age, and the baseline variables considered. Finally, 2 groups were obtained: patients with IPD and without SPA and patients with IPD and SPA.

STATISTICAL ANALYSIS

For the statistical analysis, *t*-tests for unpaired groups and the Mann-Whitney *U* test were adopted to compare the differences between the groups for the covariate variables (age, sex, and baseline variables) and to assess if a significant difference is present between the 2 groups for the primary and secondary outcome variables. Spearman correlation test was adopted to assess the correlation between the covariates and the primary outcome variables. The changes were expressed in percentage at 3 months, compared to the baseline, for maximum pain at chewing, masticatory efficiency, maximum unassisted opening, maximum assisted opening, and functional limitation. The statistical significance was set at $P < .05$, CIs: 95%.

The percentage change compared to the baseline for maximum pain at chewing was considered as the main outcome variable, and the power analysis was conducted according to a hypothesis drawn from the literature on similar patients.[41] The difference being sought between the 2 groups in the primary outcome variable, viz., pain at chewing, was 50%. Based on literature data (mean baseline value $6/10 \pm 3/10$),[28] a sample size of groups with 10 individuals in each group would warrant a statistical power of 5% for type I errors (false positive results) and 20% for type II errors (false negative results). Based on power analysis on actual data of the primary outcome variable (mean

FIGURE 6. Outflow of the saline solution through the same needle.

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FIGURE 7. Hyaluronic acid placed into the temporomandibular joint after arthrocentesis.

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baseline value 7.2 ± 2.2), the study had an 80% power to detect a 25% difference between the 2 groups.

Results

The final sample size was composed of 58 subjects with a mean age of 54.3 ± 16.5, of which 54 (93.1%) were female and 4 (6.9%) were males. Each group was composed of 29 subjects. The mean age in non-SPA and SPA groups was 54.9 ± 15.6 and 53.5 ± 17.6, respectively ($P = .7$) (Table 1). Within each group, there was the same number of males (n = 2) and females (n = 27) ($P = 1$) (Table 1). Similarly, the number of individuals undergoing bilateral arthrocentesis was 16 in both the non-SPA and SPA groups ($P = 1$) (Table 1).

The bivariate analysis of the covariates between the 2 groups, stratified by the presence or absence of SPA, shows that age, gender, and bilaterality of arthrocentesis do not have a statistically significant association with therapeutic effect, as measured with the percentage of improvement between T1 and T0 in masticatory efficiency ($P = .3$: $P = .4$; $P = .9$), maximum pain at chewing ($P = .6$; $P = .5$; $P = .8$), and maximum pain at rest ($P = .3$; $P = .3$; $P = .6$) (Table 2).

The percentage of improvement after the treatment in masticatory efficiency ($P = .8$), pain at chewing ($P = .6$), and pain at rest ($P = .9$) was not found to be significantly different in the 2 groups. No difference was found in the therapeutic effect between the non-SPA and SPA groups (Table 3).

Similarly, the mandibular functional outcomes measured according to the percentage of change from T0 to T1 in self-reported functional limitation ($P = .1$), maximum nonassisted opening ($P = .8$), and maximum assisted opening ($P = .6$) compared to baseline (T0) were not significantly different between the 2 groups after treatment (Table 4).

Discussion

The purpose of this retrospective study was to compare the outcome of arthrocentesis combined with HA in TMJ IPD patients with and without SPA.

Table 1. ALL THE STUDY COVARIATES VERSUS SPA STATUS

Covariates	IPD With SPA	IPD Without SPA	*P* Value
Age	53.52 ± 17.58	54.97 ± 15.59	.7
Sex	27 F, 2 M	27 F, 2 M	.9
Bilateral arthrocentesis	16	16	.9

Abbreviations: IPD, intra-articular pain and dysfunction; SPA, systemic polyarthritis.

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The null hypothesis was that no significant difference existed in the outcome of arthrocentesis plus HA viscosupplementation between the 2 groups. Specifically, the study aimed to evaluate whether a significant difference exists between the 2 groups for the percentage change with respect to the baseline for masticatory efficiency, maximum pain at chewing, and maximum pain at rest following the treatment. As a secondary finding, the impact of arthrocentesis on the range of motion and self-reported functional limitation was also assessed between the 2 study populations. No significant difference in improvement between the 2 groups at the 3-month follow-up was shown, suggesting that the presence of SPA does not affect the outcome of arthrocentesis in TMJ IPD patients. Based on these findings, the null hypothesis could not be rejected.

Although several studies suggested that arthrocentesis is a valuable treatment for TMJ symptoms in the context of rheumatic diseases, clinical research specifically addressing its efficacy in rheumatic patients remains limited.[42,43] Notably, this is the first study to evaluate the effects of arthrocentesis combined with viscosupplementation in a population diagnosed with SPA. The findings of the present paper are in line with a previous study by Trieger et al, which showed that arthrocentesis has a significant improvement in symptoms in a small sample of 22 females affected by rheumatoid arthritis.[30] Nevertheless, the study was limited by the lack of a control group, the impossibility of generalizing the findings to males, and the short follow-up. A confounding factor of the latter study, which is not possible to control, is the fact that subjects with rheumatoid arthritis are also under pharmacological treatment with anti-inflammatory drugs such as glucocorticoids, which could contribute as well to the improvement of the TMD status in addition to the effect of arthrocentesis. The patients included in the present investigation, in addition to joint lavage, received HA viscosupplementation, which by itself has important anti-inflammatory properties.

In the current investigation, arthrocentesis was performed via the single-needle technique proposed for the first time by Guarda-Nardini et al, which showed comparable outcomes to the two-needle technique in terms of effectiveness and tolerability.[40,41,44,45] The substances that are usually injected into the TMJ

Table 2. BIVARIATE ANALYSES OF COVARIATES VERSUS THERAPEUTIC EFFECT

	Age	Sex (M)	Sex (F)	Unilateral Arthrocentesis	Bilateral Arthrocentesis
P value	0.3	0.3		0.6	
% improvement in MPAR compared to the baseline (T0)	r = 0.13	−75 ± 50	−42 ± 73	−55.4 ± 47.6	−35.6 ± 86.6
P value	0.3	0.5		0.8	
% improvement in MPAC compared to the baseline (T0)	r = 0.15	−53 ± 42.1	−43.74 ± 43.9	−59.8 ± 46.1	−59.0 ± 40.5
P value	0.6	0.4		0.9	
% improvement in ME compared to the baseline (T0)	r = 0.06	45.6 ± 36.3	40.1 ± 68.4	32.69 ± 41.8	46.8 ± 81.5

Abbreviations: F, females; M, males; ME, masticatory efficiency; MPAC, maximum pain at chewing; MPAR, maximum pain at rest; T0, baseline; T1, follow-up.

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Table 3. BIVARIATE ANALYSES OF SPA STATUS VERSUS THERAPEUTIC EFFECT

Outcomes	T0	*P* Value	T1	*P* Value	% of Improvement Between T0 and T1 (Mean ± SD)	*P* Value
ME IPD (mean ± SD)	6.32 ± 1.8	.9	8.31 ± 1.6	.3	35.45 ± 55.68	.8
ME IPD/SPA (mean ± SD)	6.24 ± 2.4		7.62 ± 2.1		45.49 ± 76.56	
MPAC IPD (mean ± SD)	7.21 ± 2.4	.8	2.38 ± 2.8	.2	−49.64 ± 45.16	.6
MPAC IPD/SPA (mean ± SD)	7.38 ± 2.2		3.76 ± 3.5		−69.14 ± 35.36	
MPAR IPD (mean ± SD)	4.58 ± 3.8	.9	1.34 ± 2.6	.4	−35.81 ± 90.34	.9
MPAR IPD/SPA (mean ± SD)	4.69 ± 3.9		1.97 ± 2.8		−53.14 ± 46.97	

Abbreviations: IPD, intra-articular pain and dysfunction; ME, masticatory efficiency; MPAC, maximum pain at chewing; MPAR, maximum pain at rest; SPA, systemic polyarthritis; T0, baseline; T1, follow-up.

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after arthrocentesis are HA, corticosteroids, platelet-rich plasma, and human amniotic membrane.[28,46-48]

In the present study, in addition to joint lavage, patients received HA viscosupplementation, which by itself has important anti-inflammatory properties. Exogenous HA is known to increase the production of endogenous HA and exhibit chondroprotective, antioxidant, and anti-inflammatory actions in joints via suppression of interleukin (IL)-beta and IL-6 through its binding with CD44, the main HA cell surface receptor.[49-51] IL-6 is a central component in joint inflammation of some rheumatic diseases and a specific/unspecific target of several antirheumatic drugs.[52,53] Thus, it could be hypothesized that in the present study, patients with SPA could have had an additional anti-inflammatory effect from the HA injection. Moreover, it is known in general that patients with rheumatoid arthritis could have a higher prevalence of fibrotic adhesions at the level of the TMJ compared to nonrheumatic patients, and arthrocentesis is a minimally invasive procedure that can contribute to the removal of such adhesions.[26,54,55] Thus, an overlapping effect of arthrocentesis and HA could, in part, explain the optimal outcome obtained for the variables of interest.

One limitation of the present investigation is that the rheumatologic involvement of the TMJ was not specifically investigated. An inevitable limitation is related to the pharmacological treatment that patients with SPA were undergoing. Anti-inflammatory or immunosuppressive drugs could potentially affect the outcome of arthrocentesis, but ethical concerns prevented from any possibility of suspension. Thus, an overlapping effect of antirheumatic drugs and HA could explain the optimal outcome obtained for the variables of interest. The present study also has a specific follow-up period of 3 months; therefore, the results need to be confirmed in the long term. Another limitation could be related to the selection criteria: patients were randomly chosen according to their demographic characteristics and values at baseline to create groups that were as homogeneous as possible with regard to the covariates analyzed. In particular, the 2 groups had the same distribution of gender, the same number of patients undergoing bilateral or unilateral arthrocentesis, and no significant difference in mean age and baseline variables related to the TMJ IPD. While this aspect could potentially imply a selection bias, it also allowed the investigators to control

Table 4. BIVARIATE ANALYSES OF SPA STATUS VERSUS MANDIBULAR FUNCTIONAL OUTCOMES

Outcomes	T0	*P* Value	T1	*P* Value	% of Improvement Between T0 and T1 (Mean ± SD)	*P* Value
FL IPD (mean ± SD)	2.47 ± 0.7	.6	0.97 ± 1.1	.1	−37.64 ± 49.13	.1
FL IPD/SPA (mean ± SD)	2.59 ± 0.7		1.41 ± 1.1		−59.77 ± 45.16	
MNAO IPD (mean ± SD)	35.58 ± 7.4	.4	40 ± 6.2	.3	16.16 ± 22.42	.8
MNAO IPD/SPA (mean ± SD)	37.34 ± 8.3		42.03 ± 6.7		14.98 ± 19.36	
MAO IPD (mean ± SD)	38.41 ± 7.6	.3	42.69 ± 6	.2	12.10 ± 16.08	.6
MAO IPD/SPA (mean ± SD)	40.58 ± 7.8		44.69 ± 6.4		13.61 ± 18.81	

Abbreviations: FL, functional limitation; IPD, intra-articular pain and dysfunction; MAO, maximum assisted opening; MNAO, maximum non-assisted opening; SPA, systemic polyarthritis; T0, baseline; T1, follow-up.

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possible confounders that could have affected the final research outcome. Lastly, it is important to mention that the results of the present study are representative only for the outcomes of the single-needle arthrocentesis technique, with the injection of 10-50 cc of saline solution plus HA injection, and not to the continual irrigation obtained via the two-needle technique.

Given the above, it would be valuable for future studies to evaluate the effectiveness of arthrocentesis and HA in a more homogeneous population, assessing the different variables also at the joint level and not only at the patient level, and distinguishing between specific types of rheumatic diseases and possibly analyzing the correlation between the progression of TMJ status and the rheumatic disease activity by assessing by systemic inflammation markers such as the erythrocyte sedimentation rate and C-reactive protein.[56]

In conclusion, the present study showed that at 3 months of follow-up in patients with IPD and SPA, a cycle of 3 arthrocentesis plus HA contributes to a significant improvement of symptoms that is comparable to the one obtained in patients without SPA.

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