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## A one-year case series of arthrocentesis with hyaluronic acid injections for temporomandibular joint osteoarthritis

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**Objective.** The present study presents a case series on the efficacy of arthrocentesis with hyaluronic acid injections for the treatment of temporomandibular joint osteoarthritis by providing patient evaluations at a one-year follow-up.

**Study design.** Twenty-five patients with a diagnosis of osteoarthritis according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD axis I group IIIb) underwent a cycle of 5 arthrocenteses with injections (1 per week) of 1 mL hyaluronic acid. A number of clinical parameters (pain at rest and mastication, masticatory efficiency, maximum nonassisted and assisted mouth openings, functional limitation, subjective efficacy, and tolerability of the treatment) were assessed by the same blinded operator at the time of the diagnosis (baseline), at each appointment during the treatment, and at 1-week, 1-month, 3-month, 6-month, and 1-year follow-up appointments.

**Results.** Descriptive analysis showed improvements which were maintained over time for all the study parameters. Permutation tests evidenced the significance of changes which occurred in many clinical parameters within the first 2 injections. Differences with baseline levels remained significant at the end of the follow-up period, particularly for the masticatory efficiency and pain at mastication (minimum and maximum) parameters.

**Conclusions.** Data from the present investigation support findings from studies on other joints, which show the efficacy of serial injections of hyaluronic acid after arthrocentesis to reduce symptoms of osteoarthritis and to maintain improvements over time. (*Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;103:e14-e22)

Many conservative approaches to the treatment of temporomandibular disorders (TMD) have been proposed through the years, among which are occlusal splint therapy,<sup>1,2</sup> physiotherapy,<sup>3,4</sup> complimentary medicine,<sup>5,6</sup> pharmacotherapy,<sup>7,8</sup> and occlusal treatments.<sup>9</sup> The adoption of conservative treatment modalities is based on the assumption that nonreversible and invasive therapies are not indicated to treat symptoms in the absence of a well identified pathogenetic pathway.<sup>10,11</sup> For this reason, temporomandibular joint (TMJ) surgical interventions are reserved for a minority of cases, and infiltrations are usually used with caution as well. Nevertheless, recent reports have pointed out the importance of joint lubrication for a correct joint function,<sup>12</sup> also hypothesizing that abnormalities of the joint lubrication system may play a role in the onset of TMJ dysfunctions.<sup>13</sup>

Considering these premises, in the case that nonsurgical treatments fail to alleviate the symptoms, mini-

mally invasive surgical procedures were proposed with encouraging results.<sup>14-16</sup> Arthrocentesis is the simplest and less invasive among these treatments, and its use seems to be primarily indicated in the case of disc displacement without reduction.<sup>17-19</sup> The available literature data contain information about indications, success rates, prognostic risk factors, and complications rates, suggesting that patients with TMJ osteoarthritis did not respond as well as other groups of TMD patients.<sup>20-23</sup>

With the intent to extend the indications for TMJ arthrocentesis, a technique providing the injection of hyaluronic acid at the end of the articular lavage was proposed. Some studies have assessed the usefulness of hyaluronic acid infiltration techniques to improve and restore normal lubrication in joints with disc position abnormalities,<sup>24-26</sup> based on the hypothesis that a normal disc–condyle–glenoid fossa relationship depends on a low friction coefficient. Hyaluronic acid is the first choice for TMJ infiltrations because it seems to be important for joint stabilization and joint surface nutrition,<sup>13,27</sup> so its use might be useful to restore the lubrication system. Findings from those works are very promising, and treatment protocols seem to be well tolerated, so that hyaluronic acid injections have been recently proposed for the treatment of TMJ osteoarthritis as well.<sup>28,29</sup> Results from a prospective study sug-

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gest that injections of hyaluronic acid may be as effective as a conventional bite-plane therapy for the treatment of TMJ osteoarthritis, and that improvements were maintained after a 6-month follow-up.<sup>29</sup> On the basis of these observations, it was hypothesized that hyaluronic acid may reduce symptoms in osteoarthritic TMJ as well, thus overcoming the limitations of arthrocentesis alone.

Considering these premises, the present report is a 1-year case series of 25 consecutive patients with TMJ osteoarthritis treated with arthrocentesis plus hyaluronic acid injections.

## MATERIALS AND METHODS

### Study design

Criteria for inclusion in the study were the presence of a diagnosis of osteoarthritis according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD axis I group IIIb) in the absence of both RDC/TMD muscle disorders (group I diagnoses) and rheumatic diseases.

According to RDC/TMD guidelines,<sup>30</sup> a group IIIb diagnosis of osteoarthritis was made when the following signs and symptoms were present: arthralgia (TMJ pain with lateral and/or posterior palpation plus anamnestic reporting of TMJ pain during maximum voluntary mouth opening and/or maximum assisted mouth opening and/or lateral excursions); crepitus sounds; and radiologic signs of TMJ bone structures abnormalities, such as erosions, sclerosis, flattening, and osteophytes.

Twenty-five patients (23 women, 2 men; mean age 60.76 yrs; range 40-75 yrs) satisfying the inclusion criteria gave informed consent to the treatment received and took part in the study.

The study design provided a cycle of 5 arthrocenteses with injections (1 per week) of 1 mL hyaluronic acid (Hyalgan; Fidia, Abano Terme, Italy) according to the technique described by Guarda-Nardini et al.<sup>28</sup> and 5 follow-up assessments after the end of the treatment (at 1 week, 1 month, 3 months, 6 months, and 1 year).

A number of clinical parameters were assessed by the same blinded operator at the time of the diagnosis (baseline), at each appointment during the treatment, and at each appointment during the follow-up period:

- Pain at rest and mastication, assessed by means of a visual analog scale (VAS) from 0 to 10, with the extremes being “no pain” and “pain as bad as the patient ever experienced,” respectively.
- Mastication efficiency, assessed by a VAS from 0 to 10, the extremes of which were “eating only semi-liquids” and “eating solid hard food,” respectively.
- Maximum nonassisted and assisted mouth openings (in mm).

- Functional limitation during usual jaw movements (0, absent; 1, slight; 2, moderate; 3, intense, 4, severe).
- Subjective efficacy of the treatment (0, poor; 1, slight, 2, moderate; 3, good; 4, excellent).
- Tolerability of the treatment (0, poor; 1, slight, 2, moderate; 3, good; 4, excellent).

### Hyaluronic acid

Hyaluronic acid is a polysaccharide of the family of glycosaminoglycans, which can be found in many extracellular tissues, including synovial fluid and cartilage. Hyaluronic acid is produced by chondrocytes and synoviocytes of the joints, and in patients with osteoarthritis it becomes depolymerized, resulting in a decreased molecular weight and viscoelasticity. These modifications increase cartilage’s susceptibility to injuries. Exogenous hyaluronic acid can stimulate the synthesis of endogenous hyaluronic acid-forming synoviocytes of osteoarthritic joints, so reducing joint friction coefficient and decreasing risk of damage.

The hyaluronic acid used in the present investigation, Hyalgan, is a defined (500-730 kDa) molecular weight fraction of a highly purified avian sodium hyaluronate buffered (pH 6.8-7.5) in physiologic saline.

### Injection technique

The injection technique adopted in this study uses the same reference points as used in arthroscopic examination (lateral cantus-tragus). The skin surface is disinfected with povidone iodine. Local anesthesia is then achieved with 2% mepivacaine (Carbocaine; Sanofi, Winthrop, NY). The anesthetic is first injected into the joint cavity, relaxing this virtual space. Subsequently, the needle is withdrawn gently to the skin surface, thus anesthetizing the soft tissues over the joint as well. Two 19-gauge needles are then placed to make entry and exit points for the liquid to be injected that will wash out the entire joint. The arthrocentesis is performed with 50 mL Ringers lactate to eliminate the catabolites present in the synovial fluid. Once arthrocentesis is completed, 1 mL Hyalgan is injected into the joint in 3 seconds and the 2 needles are removed.

### Statistical analysis

Because observations (score variables) do not have a normal distribution and treatment effects are presumed to act possibly on more than 1 aspect, given the low sample size and the presence of nonignorable missing values in the data set, we implemented a new nonparametric permutation approach, as proposed by Pesarin,<sup>31</sup> for multivariate repeated measure problems. Standard methods may not be robust in the conditions of the present study, whereas permutation tests, based on

**Table I.** Mean and standard deviation values of minimum and maximum pain at mastication and pain at rest (VAS values) and maximum nonassisted (voluntary, MVMO) and assisted (MAMO) mouth opening in mm, before and after injections of hyaluronic acid

	1st injection	2nd injection	3rd injection	4th injection	5th injection
Pain at mastication (min)	3.56 ± 1.96	3.32 ± 2.46	2.72 ± 2.39	2.68 ± 2.51	2.04 ± 2.23
Pain at mastication (max)	7.28 ± 2.05	6.30 ± 2.62	4.92 ± 3.01	4.52 ± 3.03	4.08 ± 2.53
Pain at rest (min)	1.32 ± 2.15	1.32 ± 2.06	1.32 ± 1.80	1.36 ± 2.29	0.88 ± 1.62
Pain at rest (max)	4.36 ± 3.52	4.28 ± 3.21	3.60 ± 3.11	3.32 ± 2.87	2.60 ± 2.78
MVMO before injection	36.88 ± 8.13	37.28 ± 10.29	39.44 ± 8.35	40.08 ± 10.45	40.72 ± 8.93
MVMO after injection	39.80 ± 10.42	40.36 ± 9.95	41.68 ± 9.16	41.40 ± 8.84	41.84 ± 8.09
MAMO before injection	41.24 ± 9.12	41.96 ± 11.45	42.92 ± 9.15	43.8 ± 11.10	44.76 ± 9.52
MAMO after injection	43.40 ± 10.72	44.60 ± 10.77	45.24 ± 9.42	45.76 ± 9.85	46.04 ± 9.24

combining dependent permutation tests, have been shown to be effective and to provide robust and exact solutions. The purpose of the present analysis was to evaluate the treatment effects both during the cycle of injections and during the follow-up period. Therefore, the null hypothesis of interest is that the variables have the same joint distribution with respect to time, i.e., they have null treatment effect, and we wished to test if the treatment had an appreciable improvement (increasing or decreasing) on the variables. We created a design matrix for repeated measure analysis that considers all possible comparisons (contrasts). All tests were performed using Matlab routines, the number of permutation are set to 5000, and to combine  $P$  values with respect to time within each variable we used the Tippett combining function.

Descriptive results are reported in Tables I (injections period) and II (follow-up period). Figures 1-10 refer to pain at mastication, pain at rest, and maximum voluntary and assisted mouth opening values during the injection period. Figures 11-14 refer to the same values during the follow-up period.

## RESULTS

### Pain at mastication

The reported baseline mean minimum and maximum pain values during mastication were  $3.56 \pm 1.96$  and  $7.28 \pm 2.05$ , respectively. Both values decreased after the second hyaluronic acid injection, and at the time of the third appointment the values were  $2.72 \pm 2.39$  and  $4.92 \pm 3.01$ , respectively. The change in VAS values from the first to the third injection that can be observed graphically is also confirmed by significant  $P$  values:  $P = .0316$  for minimum pain at mastication, and  $P = .0016$  for maximum pain. Mean VAS values of pain at mastication kept on decreasing to the end of treatment. At the last injection, values were  $2.04 \pm 2.23$  and  $4.08 \pm 2.53$  for minimum and maximum pain at mastication, respectively; there was a significant decrease from the first to the fifth injection in both minimum

( $P = .0004$ ) and maximum ( $P = .0002$ ) pain at mastication.

Considering the whole cycle of 5 injections, using the nonparametric combination methodology of the  $P$  values with respect to time, there is a significant decrease of the values assumed by the parameter minimum pain at mastication ( $P = .0018$ ) and maximum pain at mastication ( $P = .0010$ ).

Regarding the follow-up period, at 1 week the follow-up values were  $1.80 \pm 2.14$  and  $3.48 \pm 2.47$ , respectively, and values kept on decreasing to the end of follow-up period: At 1 year, the mean minimum pain at mastication was  $0.80 \pm 1.47$  and the maximum was  $2.58 \pm 2.47$ . The change in values from the first to the fifth follow-up was significant ( $P = .0170$  for minimum pain at mastication;  $P = .0462$  for maximum pain at mastication). As described for the cycle of 5 injection, by using the nonparametric combination methodology with respect to time, globally there was an improvement in terms of decreasing VAS values:  $P = .0268$  for minimum pain at mastication, and  $P = .0378$  for maximum pain at mastication.

### Pain at rest

The pretreatment mean minimum and maximum pain levels at rest were  $1.32 \pm 2.15$  and  $4.36 \pm 3.52$ , respectively. A significant reduction in the mean maximum pain at rest values emerged at the time of the fifth injection (mean value  $2.60 \pm 2.78$ ); comparing the VAS values at the first injection with those at the last injection, a decrease with  $P = .0062$  was shown. When we considered the whole cycle of 5 injections, using the nonparametric combination methodology of the  $P$  values with respect to time, globally there was a significant decrease in the values assumed by the parameter maximum pain at rest ( $P = .0236$ ). On the other hand, the mean minimum pain at rest values decreased more slowly, and at the time of the end of the treatment the mean value was  $0.88 \pm 1.62$  and changes were not significant. Mean VAS values of pain at rest kept on

**Table II.** Mean and standard deviation values of minimum and maximum pain at mastication and pain at rest (VAS values) and maximum nonassisted (voluntary, MVMO) and assisted (MAMO) mouth opening in mm

	1st follow-up	2nd follow-up	3rd follow-up	4th follow-up	5th follow-up
Pain at mastication (min)	1.80 ± 2.14	1.28 ± 1.79	0.96 ± 1.54	0.80 ± 1.22	0.80 ± 1.47
Pain at mastication (max)	3.48 ± 2.47	2.88 ± 2.71	2.84 ± 2.46	2.36 ± 2.10	2.58 ± 2.47
Pain at rest (min)	0.24 ± 1.01	0.20 ± 0.71	0.20 ± 0.65	0.24 ± 0.66	0.64 ± 1.29
Pain at rest (max)	1.64 ± 2.50	1.48 ± 2.24	2.00 ± 2.47	1.60 ± 2.25	1.54 ± 2.05
MVMO	42.2 ± 6.95	42.88 ± 7.61	42.68 ± 7.49	42.6 ± 7.79	42.44 ± 8.51
MAMO	45.8 ± 7.92	46.12 ± 8.33	46.08 ± 8.34	45.84 ± 8.25	47.08 ± 9.00

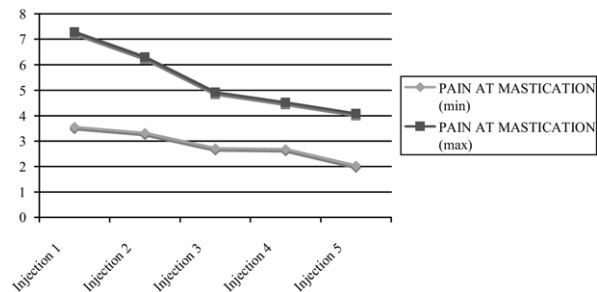


Fig. 1. Mean values of minimum and maximum pain at mastication (VAS).

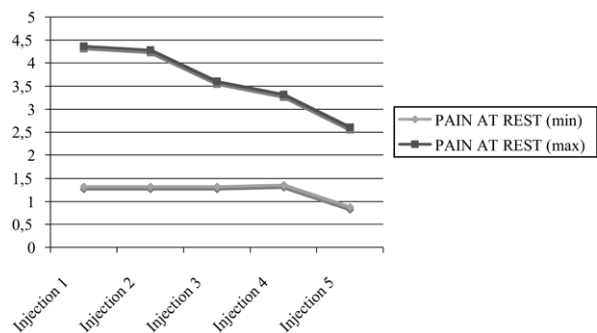


Fig. 2. Mean values of minimum and maximum pain at rest (VAS).

decreasing to the end of the follow-up period for both maximum (mean 1.54 ± 2.05) and minimum pain levels (mean 0.64 ± 1.29), but this decrease was not significant.

**Masticatory efficiency**

The mean masticatory efficiency VAS value at baseline was 5.74 ± 2.11 (range 1.5-10). After the first 4 injections masticatory efficiency did not improve significantly, but changes became significant with the fifth injection (mean 6.84 ± 1.95). When we compared the first injection with the last one, a significant increase in VAS values ( $P = .005$ ) was noticed, and the same

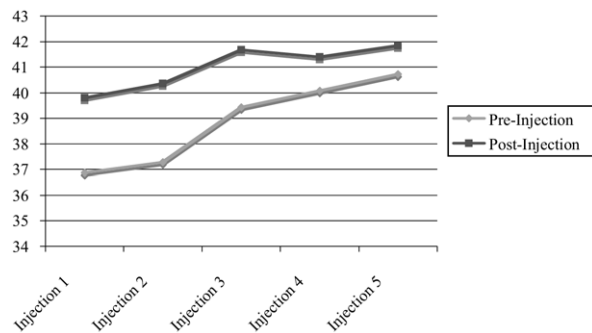


Fig. 3. Mean values of maximum nonassisted (voluntary) mouth opening (MVMO) in mm, before and after injection.

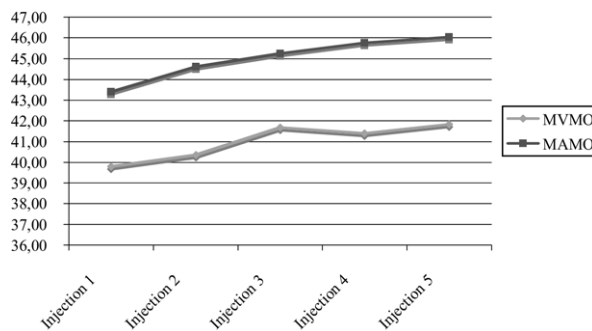


Fig. 4. Mean values of maximum assisted (MAMO) mouth opening in mm, before and after injection.

happens when comparing the second, the third, and the fourth injection with the fifth one:  $P = .0018$ ,  $P = .0022$ , and  $P = .0382$ , respectively. A global improvement in terms of increase ( $P = .0120$ ) was shown. Efficiency of mastication kept on improving after the end of treatment. Regarding the follow-up period, at the 1-week follow-up (the first one) mean VAS value was 7.44 ± 1.79 and at the 1-year follow-up (the last one) mean VAS value was 7.98 ± 1.40. A significant variation from the first to the third follow-up ( $P = .0128$ ) and from the first to the fourth follow-up ( $P = .0134$ ) emerged.

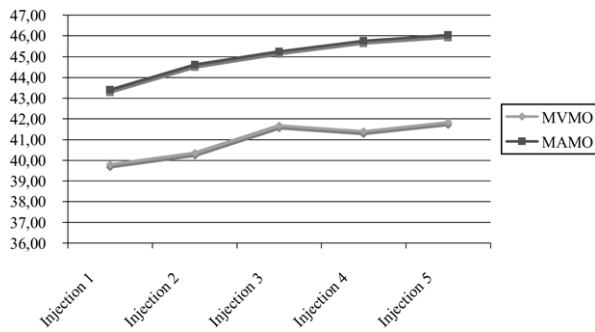


Fig. 5. Mean values of maximum nonassisted (voluntary, MVMO) and assisted (MAMO) mouth opening in mm, after injection.

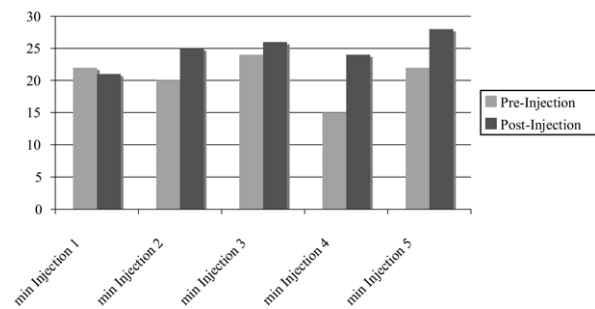


Fig. 6. Minimum nonassisted mouth opening. Pre- and postinjection values.

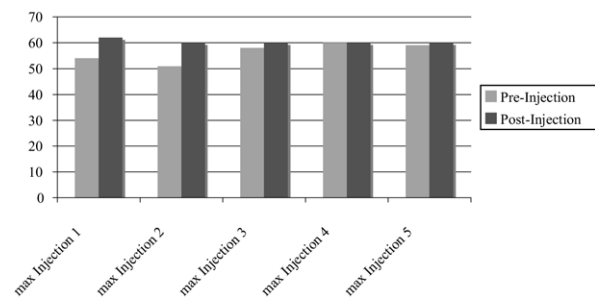


Fig. 7. Maximum nonassisted mouth opening. Pre- and postinjection values.

### Maximum nonassisted mouth opening

The mean maximum nonassisted opening (in mm) at baseline time was  $36.88 \pm 8.13$  (range 22-54). Significant improvements were noticed immediately after the first injection, with a postinjection mean value of  $39.80 \pm 10.42$  (range 21-62). Using nonparametric permutation methods for paired samples, we noticed that the difference between before and after the first injection was significant ( $P = .0008$ ). A similar signif-

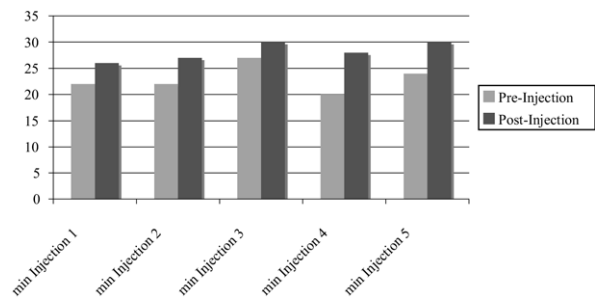


Fig. 8. Minimum assisted mouth opening. Pre- and postinjection values.

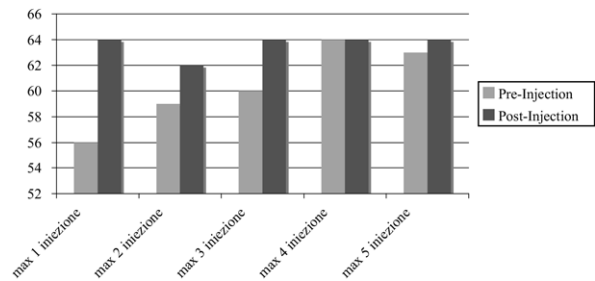


Fig. 9. Maximum assisted mouth opening. Pre- and postinjection values.

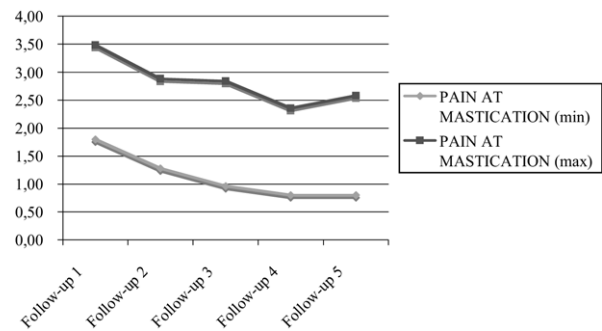


Fig. 10. Mean values of minimum and maximum pain at mastication (VAS).

icant positive effect was reported for the second ( $P = .0016$ ) and the third ( $P = .0004$ ) injections, and at the end of the treatment period the maximum nonassisted mouth opening was  $41.84 \pm 8.09$  (range 28-60), significantly higher than the pr-treatment value ( $P = .0278$ ). Combining these  $P$  values, there was a global improvement on maximum nonassisted mouth opening ( $P = .0012$ ). The improvements obtained with the treatment were maintained during the follow-up period, at the end of which the mean maximum nonassisted opening was  $42.44 \pm 8.51$  (range 30-59).



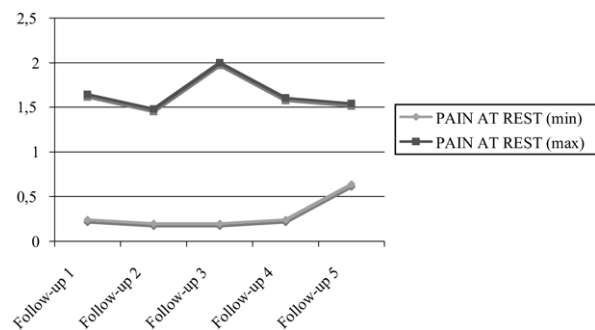


Fig. 11. Mean values of minimum and maximum pain at rest (VAS).

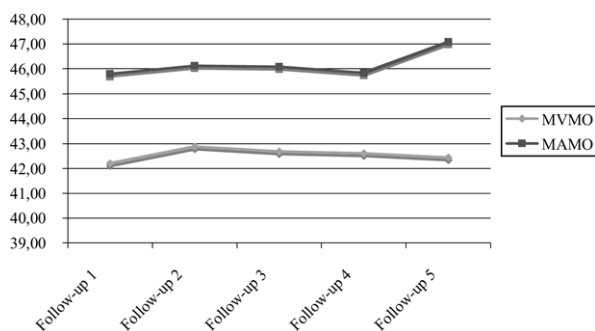


Fig. 12. Mean values of maximum nonassisted (voluntary, MVMO) and assisted (MAMO) mouth opening in mm.

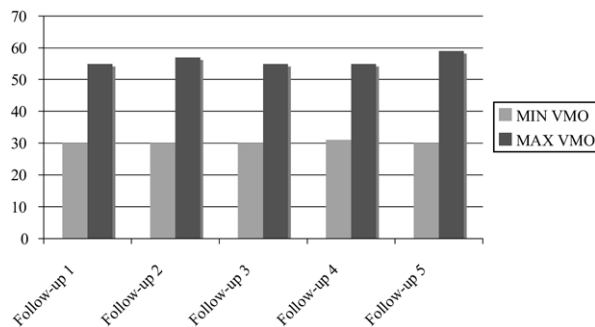


Fig. 13. Minimum and maximum nonassisted (voluntary) mouth opening values.

### Maximum assisted mouth opening

At the first injection, the mean pretreatment maximum assisted mouth opening (in mm) was  $41.24 \pm 9.12$  (range 22-56) and the postinjection value was significantly higher ( $43.4 \pm 10.72$ ;  $P = .0096$ ). The same significant improvement was shown for all of the injections. At the fifth injection, the mean pretreatment value was  $44.76 \pm 9.52$  and the posttreatment value

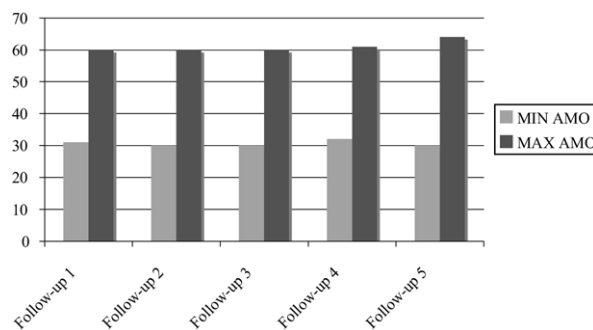


Fig. 14. Minimum and maximum assisted mouth opening values. One missing value in the last follow-up.

was  $46.04 \pm 9.24$  ( $P = .0244$ ). The global  $P$  value was .0008. The mean maximum assisted mouth opening value kept on improving during the follow-up period, reaching the value of  $47.08 \pm 9.00$  (range 30-64) at the 1-year follow-up.

### Functional limitation

The mean functional limitation score at baseline time was  $2.62 \pm 0.86$ . The mean score kept on decreasing during the treatment, and at the end of the cycle of injections mean score was  $1.58 \pm 0.89$ . At the end of the follow-up period the mean score was  $1.30 \pm 0.90$ . There was a significant decrease during the treatment in almost all of the comparisons between injections, and in particular a  $P$  value of .0002 emerged in the comparison between the first and the last injection. When we considered the whole cycle of 5 injections, using the nonparametric combination methodology of the  $P$  values with respect to time, globally there was a significant decrease in the values assumed by the parameter functional limitation ( $P = .0012$ ).

### Efficacy of the treatment

Eight patients (32%) reported a good subjective efficacy of the treatment after the second injection (mean score  $1.74 \pm 1.13$ ). At the end of the 5-injection protocol the mean score was  $2.64 \pm 0.90$ , with 12 patients (48%) considering at least “good” the subjective efficacy of the treatment. The number of patients reporting an “excellent” subjective efficacy rose to 9 (36%) at the end of the follow-up period (mean score  $2.82 \pm 1.23$ ). The subjective efficacy of the treatment improved significantly during the cycle of the injection and, combining  $P$  values, a global increase in subjective efficacy values ( $P = .0040$ ) emerged. The same thing did not happen for follow-up assessments, where no significance was found.

### Tolerability of the treatment

Twelve patients (48%) considered “good” the tolerability of the first injection, and 2 (8%) reported a “poor” tolerability, with a mean score of  $2.48 \pm 1.08$ . The tolerability of the treatment did not change significantly over time, and the mean score at the end of the treatment period was  $2.36 \pm 0.99$ ; 13 patients (52%) considered the tolerability to be “good,” 2 (8%) “poor,” and 1 (4%) “excellent” at the end of the cycle of injections. At the first follow-up assessment, the mean score was  $2.66 \pm 0.97$ , and 10 patients (40%) considered the tolerability to be “good,” 1 (4%) “poor,” and 5 (20%) “excellent.”

### DISCUSSION AND CONCLUSIONS

The present prospective study assessed the efficacy at 1 year of a cycle of hyaluronic acid injections performed immediately after arthrocentesis for the treatment of osteoarthritic TMJs. A similar approach to TMJ pathologies is justified by recent observations indicating that an increase in joint friction coefficient is a main risk factor for degenerative joint pathologies<sup>12,13</sup> and that hyaluronic acid, being an essential component for joint lubrication, may help in reducing joint friction.<sup>27,32</sup>

Such a hypothesis seems to be supported by experimental data on porcine TMJs, which suggest that lubrication by means of hyaluronic acid decreases friction in joints with experimentally abraded cartilage surfaces by approximately 50%,<sup>32,33</sup> and on ovine TMJs, which suggest hyaluronic acid is better than physiologic saline for the inhibition of osteoarthritis.<sup>34</sup>

Moreover, some preliminary findings gave encouraging results, and literature data are available on the efficacy of intra-articular hyaluronic acid injections in patients with disc displacement with reduction,<sup>25</sup> with disc displacement without reduction,<sup>24,35</sup> and with osteoarthritis.<sup>28,29</sup> In contrast, an older double-blind placebo-controlled clinical trial reported that injections of hyaluronic acid may be effective to reduce symptoms at 6-months in subjects with reducing disc displacement but not in patients with degenerative joint diseases.<sup>36</sup>

The most effective protocol seems to be the combination of arthrocentesis and hyaluronic acid injection,<sup>26</sup> repeated for a cycle of 5 injections (1 per week).<sup>28</sup> The choice of adopting a treatment protocol based on a cycle of 5 injections was based on the positive findings described with a similar approach to other joints. Studies on patients with osteoarthritis of the knee described significant improvements in patients' symptoms and showed that the cycle of 5 injections was the most effective to maintain them over time.<sup>37-39</sup>

In the present study, such a protocol was applied to 25 patients with osteoarthritis of the TMJ, as diagnosed

according to the RDC/TMD.<sup>21</sup> This classification system was adopted for the first time in studies on TMJ arthrocentesis in the attempt to introduce standardization of TMD diagnosis, as already applied to studies on TMD epidemiology.<sup>40-43</sup>

A wide range of objective (maximum nonassisted and assisted mouth openings and protrusive and laterotrusive movements) and subjective (pain at rest, pain at mastication, mastication efficiency, functional limitation, subjective efficacy of the treatment, and tolerability of the treatment) parameters were assessed to evaluate treatment efficacy, and significant improvements were reported especially in minimum and maximum pain at mastication, maximum pain at rest, masticatory efficiency, and functional limitation during the treatment. Furthermore, the improvements achieved during the treatment were maintained over the follow-up period, in particular for masticatory efficiency and minimum and maximum pain at mastication.

This study has a number of limitations, the first of which is represented by the absence of a control group in which only the injections of hyaluronic acid or only the arthrocentesis was performed. The lack of an active control group makes it impossible to determine which is the effective part of the protocol (i.e., if hyaluronic acid injections are mainly responsible for symptom improvement).

Nevertheless, in the absence of consistent literature on TMJ osteoarthritis, we chose to apply the same protocol adopted to test the efficacy of arthrocentesis combined with hyaluronic acid in other joints. On the basis of literature data, serial injections seem to be effective to maintain improvements over time, and a similar effect may be supposed for osteoarthritic TMJs. Controlled trials have suggested that a treatment protocol providing both arthrocentesis and hyaluronic acid injections is superior to arthrocentesis alone to control symptoms in patients with nonreducing TMJ disk displacement over a 2-year follow-up period.<sup>26</sup>

The main target of the present investigation was to gather preliminary data on the efficacy of the same protocol that appears to be the most effective in patients with nonreducing disc displacement<sup>26</sup> and osteoarthritis.<sup>28,29</sup>

As in the case of the other TMDs, in patients with osteoarthritis most parameters improved markedly within the first 2 injections, and improvements became slower during the rest of the treatment period. These findings may suggest a lack of effectiveness of serial injections of hyaluronic acid in the osteoarthritic TMJ, indicating that a smaller amount of injections may be effective to alleviate symptoms of osteoarthritis.

These considerations clearly suggest that controlled trials are strongly needed with the 2-fold objective of

testing the relative effectiveness over time of different protocols and comparing the relative effectiveness of hyaluronic acid injections after arthrocentesis with arthrocentesis alone, placebo or other intrarticular medications, such as corticosteroids.

In conclusion, data from the present investigation supported the usefulness of serial hyaluronic acid injections performed after arthrocentesis for the treatment of TMJ osteoarthritis and for the maintenance of improvements over a 1-year follow-up period in a case series of 25 patients. Besides, the treatment protocol was well tolerated by the patients, who also reported a good subjective efficacy. These findings need to be re-evaluated by future researches with an appropriate design to overcome the present study's limitations.

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