

Effectiveness of treatment with viscosupplementation in temporomandibular joints with or without effusion

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L. Guarda-Nardini, A. Rossi, R. Ramonda, L. Punzi, G. Ferronato, D. Manfredini: Effectiveness of treatment with viscosupplementation in temporomandibular joints with or without effusion. *Int. J. Oral Maxillofac. Surg.* 2014; 43: 1218–1223. © 2014 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. The objective of this study was to determine whether the effectiveness of viscosupplementation with hyaluronic acid (HA) in patients with temporomandibular joint (TMJ) degenerative disorders depends on the presence of intra-articular effusion. In this study of case-control design, two groups of 25 patients were recruited: patients with a clinical diagnosis of painful chronic TMJ osteoarthritis and magnetic resonance imaging (MRI) signs of TMJ degeneration, with (effusion group) or without (no effusion group) MRI evidence of TMJ effusion. All patients underwent five weekly single-needle arthrocenteses plus medium molecular weight HA and 6 months of follow-up. Several clinical outcome parameters were assessed. For all variables, analysis of variance (ANOVA) for repeated measures was performed to assess the existence of significant within-group and between-group treatment effects. Over time, both groups showed significant improvements in all outcome parameters, which were maintained at the 6-month follow-up ($P < 0.05$). Between-group comparisons showed that the treatment effects did not differ significantly for either the primary outcome variable (pain levels: $F = 0.849$, $P = 0.548$) or secondary outcome variables (chewing efficiency: $F = 0.854$, $P = 0.544$; functional limitation: $F = 1.35$, $P = 0.226$; mouth opening: $F = 0.658$, $P = 0.707$). The null hypothesis that there are no differences in treatment effectiveness between patients with and without effusion could not be rejected.

Keywords: temporomandibular joint osteoarthritis; hyaluronic acid; viscosupplementation; arthrocentesis; effusion.

Accepted for publication 1 May 2014
Available online 2 June 2014

Degenerative disorders of the temporomandibular joint (TMJ) are a common cause of pain and treatment-seeking behaviour in the field of orofacial pain, and

require careful diagnostic assessment and therapeutic planning.¹ Among the various strategies that have been proposed over the years to manage pain and improve

function, viscosupplementation with hyaluronic acid (HA) injections has been gaining widespread attention.² The introduction of this approach within the practice of TMJ

disorders has resulted from the progressive evolution and modification of the first works on TMJ arthrocentesis,^{3–5} as well as to a parallel increase in knowledge about the potential application of HA to manage osteoarthritis (OA) of the larger joints.^{6,7}

The potential role of impairment in joint lubrication as a risk factor for TMJ internal derangements and subsequent inflammatory–degenerative disorders has provided a rationale for TMJ viscosupplementation,⁸ and several clinical studies have shown that it may be an effective treatment modality.^{9–12} Nevertheless, a recent review pointed out that, despite seemingly encouraging findings at the study population level, much information is yet to be gathered on the most suitable protocol and indications at the individual level.¹³ Since then, several clinical trials have been conducted by our research group to collect data on the most effective number of injections, the ideal HA molecular weight, and, more in general, on the predictive factors for clinical symptom improvement.^{14–18}

An issue that is worthy of exploration is the effect of joint effusion on the effectiveness of viscosupplementation treatment, based on reports from studies on the larger joints (i.e. knee, hip) indicating that protocols of HA injections may not be of benefit in the presence of intra-articular effusion.^{19,20} This issue has not been addressed so far in the TMJ literature; hence exploratory trials on this subject may provide additional useful information to tailor the treatment of TMJ degenerative disorders.

Based on these premises, the aim of the present investigation was to answer the clinical research question: in patients with TMJ degenerative disorders, does the effectiveness of viscosupplementation with hyaluronic acid depend on the presence of intra-articular effusion? The null hypothesis was that there are no differences in treatment effectiveness between patients with and without effusion. To test the hypothesis, the investigators assessed treatment-related changes in certain clinical outcome variables in two groups of patients with painful TMJ degenerative disorders, those with and without magnetic resonance imaging (MRI) signs of TMJ effusion.

Materials and methods

To address the research purpose, the investigators designed a clinical trial by recruiting patients seeking treatment at the temporomandibular disorders clinic of the study institution. The study population



Fig. 1. Example MRI for patients in the ‘effusion’ group, showing internal derangement with anterior disc displacement, condylar cortical bone erosion, and a large fluid effusion (white area) in the anterosuperior joint compartment at closed mouth.

was composed of patients aged between 40 and 60 years with a clinical diagnosis of OA (Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) version 1.0–axis I group IIIb)²¹ and with joint pain lasting for more than 6 months. All patients had to have MRI signs of TMJ degeneration.²² Based on recent findings showing the influence of psychosocial factors on treatment effectiveness,¹⁸ patients with RDC/TMD axis II high levels of pain-related impairment were excluded from the study.

The sample size required for the investigation was ascertained. The primary outcome variable was treatment effectiveness based on the assessment of pain levels on a 10-point visual analogue scale (VAS) with 0 being the absence of pain and 10 being the worst pain ever. Previous calculations in the literature based on investigations with similar study populations, assuming a mean VAS value of $6/10 \pm 3/10$ for the main outcome variable (i.e. pain levels), have shown that 40 subjects are needed to detect an approximate 40% between-groups difference in mean pain for chewing VAS values, with a statistical power of 5% for type I error (i.e. false-positive results) and 20% for type II error (i.e. false-negative results).¹⁶ Thus, to further increase the statistical power, 50 patients were recruited for the present investigation.

Using a case–control study design, patients were split into two groups, one with MRI signs of effusion and one without effusion (Figs. 1 and 2). Joint effusion was identified in T2- or DP-weighted images as a large area of high signal intensity inside the joint space. More specifically, in accordance with the hypothesis that a mild to moderate amount of fluid can be detected in normal joints as well, the presence of effusion was defined as the presence of areas of high signal

intensity greater than 2 mm in superior–inferior height or anterior–posterior length inside the articular space.²³ To avoid interpretation bias related to the assessment of images by different radiologists, the MRI were interpreted by the expert clinicians of this investigation (DM and LGN), who recorded the presence/absence of effusion and disc position abnormalities by consensus.

Patients were recruited consecutively until the target population of 25 subjects per group was attained. Both groups of patients underwent five weekly single-needle arthrocenteses plus medium molecular weight HA and 6 months of follow-up. Patients were instructed to have a 2-week wash out period before starting the treatment protocol and not to use medications on a routine basis during the active treatment and follow-up periods (i.e. only paracetamol 1000 mg was allowed in the immediate post-intervention phases).



Fig. 2. Example MRI for patients in the ‘no effusion’ group, showing severe degeneration of the condylar head, without areas of effusion.

The single-needle technique refers to the approach first described by Guarda-Nardini et al.,²⁴ in which only one needle is used for both saline fluid injection and ejection. The technique was performed under local anaesthesia and an average of approximately 10 ml saline was used for joint lavage. After joint lavage, patients received 1 ml medium molecular weight, i.e. 1200 kDa, hyaluronic acid (Sinovial; IBSA Farmaceutici, Lodi, Italy).

For each patient, along with the primary outcome variable, a number of secondary outcome parameters were assessed, including subjective chewing efficiency (0–10 VAS scale with 0 being the worst efficiency ever and 10 the best efficiency ever), functional limitation on a five-point scale (with 0 being the lowest and 4 the maximum value), and jaw range of motion function in millimetres. All the outcome variables were evaluated at baseline, at each intervention appointment, at the end of treatment, and at the 3-month and 6-month follow-up appointments after the end of treatment. Treatment tolerability and perceived subjective treatment effectiveness were also assessed on a five-point scale. All interventions were performed by one of the two main investigators (DM and LGN), and the outcome parameters were recorded by the same physician (AR) who was fully blinded to the group to which the patient belonged.

In an attempt to minimize bias related to the patients' knowledge of their joint status, the patients received only basic counselling about their need to undergo TMJ injections, without any further specifications on the potential difference in benefit of administering arthrocentesis plus HA injections in joints with or without effusion. All patients gave their written consent to the intervention, and the study was approved by the institutional review board and medical directorate.

For statistical purposes, VAS pain levels and jaw range of motion values were managed as continuous variables, while data on subjective efficacy and tolerability levels were managed as ordinal variables. For all variables, analysis of variance (ANOVA) for repeated measures was performed to assess the existence of significant within-group and between-group treatment effects. For all comparisons, statistical significance for differences was set at $P < 0.05$.

Results

The demographic characteristics were matched between the two groups. The 'effusion' group included 21 females

Table 1. Baseline between-group comparison of the outcome variables ($P > 0.05$ for all the parameters).

Outcome variable	No effusion group	Effusion group
Pain levels (0–10)	6.4 ± 0.6	6.1 ± 0.7
Chewing efficiency (0–10)	6.5 ± 0.5	5.8 ± 0.6
Functional limitation (0–4)	2.3 ± 0.2	2.4 ± 0.2
Mouth opening (mm)	39.4 ± 2.1	37.2 ± 2.5

and four males, and the 'no effusion' group included 20 females and five males; mean age was 48.2 ± 11.7 years and 45.4 ± 9.9 years, respectively ($P = 0.560$).

At baseline, the two groups showed no significant difference in any outcome variable ($P > 0.05$) (Table 1). There were no drop-outs during the treatment period or follow-up. No clinically relevant side effects were noted in any patient, with the exception of mild swelling in one patient in the 'no effusion' group the day after the first injection.

Over time, both groups showed significant improvements in all of the outcome

parameters, which were maintained at the 6-month follow-up ($P < 0.05$). Between-group comparisons showed that the treatment effects did not differ significantly for either the primary outcome variable (pain levels: $F = 0.849, P = 0.548$) or the secondary outcome variables (chewing efficiency: $F = 0.854, P = 0.544$; functional limitation: $F = 1.35, P = 0.226$; mouth opening: $F = 0.658, P = 0.707$) (Figs. 3–6).

Also, no significant difference was detected between the two groups for the subjective perceived efficacy ($P = 0.991$). In addition, the treatment protocol was tolerated similarly by the patients in both groups ($P = 0.849$) (Table 2).

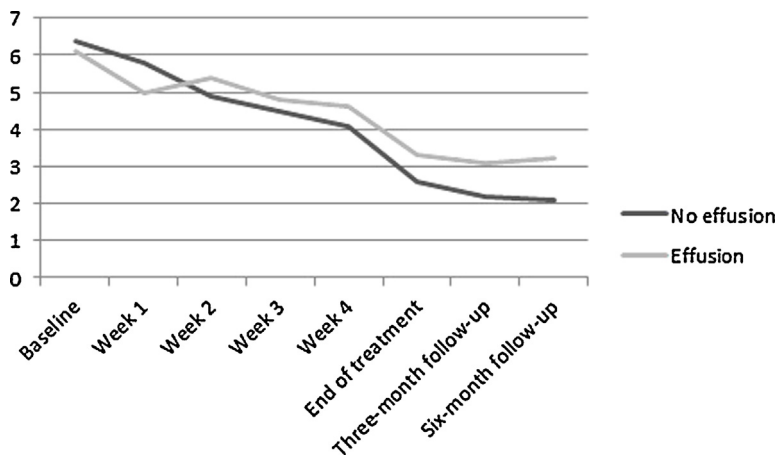


Fig. 3. Changes in pain levels over time in the two study groups, as measured on a 0–10 VAS rating scale (expected change was a decrease).

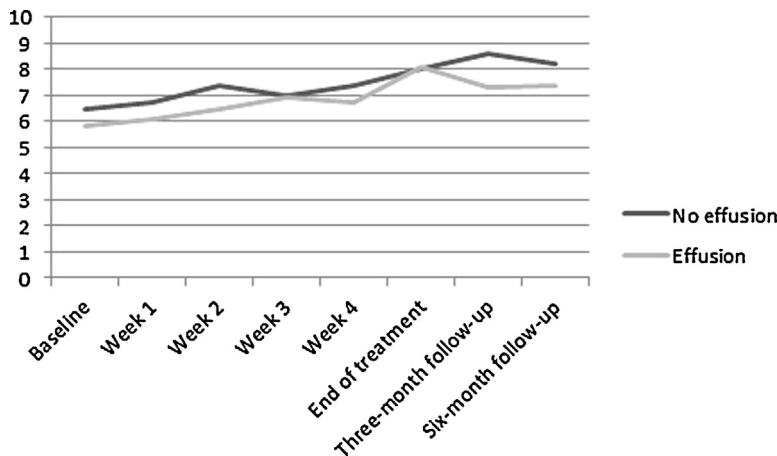


Fig. 4. Changes in chewing efficiency levels over time in the two study groups, as measured on a 0–10 VAS rating scale (expected change was an increase).

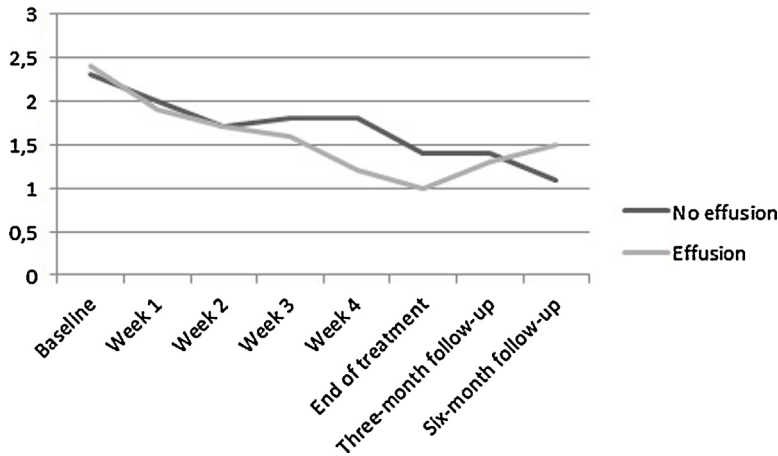


Fig. 5. Changes in functional limitation levels over time in the two study groups, as measured on a 0–4 scale (expected change was a decrease).

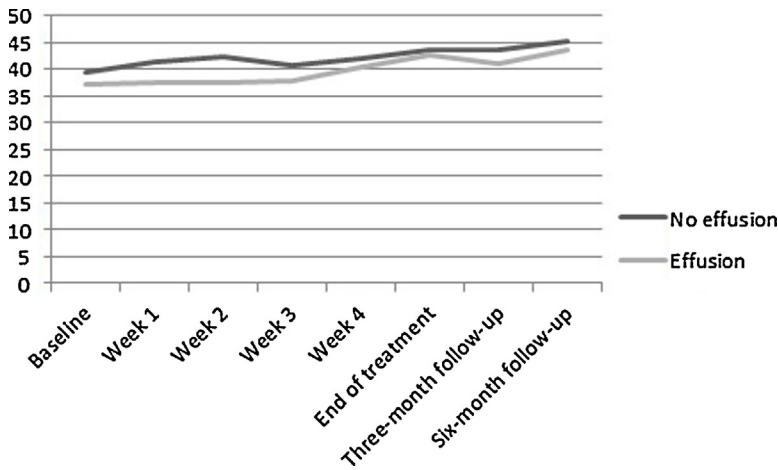


Fig. 6. Changes in mouth opening values over time in the two study groups, as measured in millimetres (expected change was an increase).

Taken together, the findings did not allow the rejection of the null hypothesis that there are no differences in treatment effectiveness between patients with and without effusion.

Discussion

Since their introduction to the field of TMJ disorder practice, there has been a progressive expansion in the clinical indications for strategies to provide viscosupplementation to the TMJ, particularly with regard to joints with inflammatory–degenerative disorders.^{5,9,11,25} Protocols for symptom management in the larger joints led to the immediate adoption of the cycle of five

weekly HA injections, and encouraging findings soon emerged from long-term case series involving patients with TMJ disorders.^{9,10} A previous clinical trial from our research group also supported the superiority of multiple-injection protocols with respect to single-session joint lavage.¹⁵ Thus, this five-session protocol has been used in many studies as the standard of reference when attempting to gain deeper knowledge of the many issues concerning the predictability of HA viscosupplementation at the individual level.

In the present investigation, the hypothesis that the effectiveness of treatment may be different in subjects with TMJ degenerative disorders with or without

effusion was assessed. The rationale for this hypothesis was that the presence of intra-articular effusion may negatively influence the therapeutic properties of the injected HA. Indeed, there is contradictory clinical evidence of the effectiveness of viscosupplementation strategies in joints with fluid accumulation, such as those featuring MRI effusion. For instance, investigations on knee OA suggested that clinical symptoms in patients with joints with effusion improved less than in patients with joints without effusion, and, more in general, that viscosupplementation is not indicated or should not be the primary option in the active phases of the arthritic flare.^{19,26} In contrast, the effectiveness of treatment in hip OA appears to be less influenced by the presence of joint effusion,²⁷ even if there is agreement among researchers that several issues are yet to be resolved before conclusions can be drawn on this topic.²⁰

The findings from this investigation clearly showed that the effectiveness at 6 months was not significantly different between patients with TMJ degenerative disorders with and without effusion. There were significant improvements in all of the subjective (i.e. pain levels, chewing efficiency, functional limitation, subjective perceived efficacy) and objective (i.e. mouth opening values) outcome parameters for both groups of patients. The treatment protocol was equally tolerated by the two groups. Nevertheless, it must be pointed out that a tendency for a partial decrease in effectiveness in joints with effusion from the 3-month to the 6-month follow-up was shown for pain levels and functional limitation, possibly suggesting that a longer follow-up period may be an interesting addition in future studies to confirm or refute these findings.

Based on the above, this investigation suggests that the presence of MRI evidence of intra-articular effusion is not a critical factor for the effectiveness of treatment with HA injections, thus adding data to the controversial larger-joint literature on the topic. From an anatomical and biological viewpoint, there is no reason to hypothesize that the TMJ will have a different response to treatment compared to, for instance, the knee, and that this in turn may react differently with regards to the hip. So, another rationale to explain our results should be found.

The most plausible hypotheses relate to both the methodological design of this investigation and the technique for TMJ injections adopted here. Indeed, from a methodological viewpoint, one cannot ignore the possibility that previous findings

Table 2. End of treatment between-group comparison for subjective perceived efficacy and tolerability of the treatment (*P* > 0.05 for both parameters).

Outcome variable	No effusion group	Effusion group
Perceived efficacy (0–4)	2.5 ± 0.8	2.5 ± 1.1
Treatment tolerability (0–4)	2.4 ± 1.2	2.4 ± 1.1

on larger joints could have been influenced by the inclusion of patients with different pain-related psychosocial impairment, which has been shown to be a critical factor in the prediction of the effectiveness of treatment with TMJ viscosupplementation.¹⁸ As for the clinical technique, it has been suggested as a result of studies on larger joints, that joint lavage and fluid aspiration, as performed in this investigation, is indicated to increase treatment effectiveness in inflamed joints.²⁸ The additional value of combined joint lavage and viscosupplementation with HA has also been shown in previous studies to be superior to the single techniques, i.e. joint lavage or viscosupplementation, in TMJ disorders.^{15,29} Of course, a shortcoming of the present study is the absence of a control group undergoing arthrocentesis alone, and this prevents us from confirming or refuting the superiority of the combined protocol over the single techniques in osteoarthritic TMJs with effusion. Future studies addressing this interesting topic are thus needed, although a true comparative trial would be hard to perform due to ethical concerns about the actual need to perform five joint lavages without the purported active part of the treatment, i.e. the hyaluronic acid.

In conclusion, our findings show that in a population of patients with TMJ degenerative disorders without psychosocial impairment, the presence of MRI signs of intra-articular effusion did not influence the effectiveness of a treatment protocol of five-session joint viscosupplementation immediately following lavage.

Funding

None.

Competing interests

None of the authors have any conflicts of interest to declare and no financial support was received for the present investigation.

Ethical approval

This study was approved by the Institutional Review Board of the University of Padova.

Patient consent

Not required.

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