Myofascial Pain of the Jaw Muscles: Comparison of Short-Term Effectiveness of Botulinum Toxin Injections and Fascial Manipulation Technique

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0886-9634/3002-000$05.00/0, THE JOURNAL OF CRANIOMANDIBULAR PRACTICE,

Manuscript received March 2, 2011; revised manuscript received November 29, 2011; accepted November 29, 2011

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ABSTRACT: A randomized controlled trial was performed to compare the short-term effectiveness of botulinum toxin injections and physiatric treatment provided by means of Fascial Manipulation (a technique licensed by and registered to Luigi Stecco) techniques in the management of myofascial pain of jaw muscles. Thirty patients with a Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) diagnosis of myofascial pain were randomized to receive either single-session botulinum toxin injections (Group A) or multiple-session Fascial Manipulation (Group B). Maximum pain levels (VAS ratings) and jaw range of motion in millimeters (maximum mouth opening, protrusion, right and left laterotrusion) were assessed at baseline, at the end of treatment, and at a three-month follow-up. Both treatment protocols provided significant improvement over time for pain symptoms. The two treatments seem to be almost equally effective, Fascial Manipulation being slightly superior to reduce subjective pain perception, and botulinum toxin injections being slightly superior to increase jaw range of motion. Differences between the two treatment protocols as to changes in the outcome parameters at the three-months follow-up were not relevant clinically. Findings from the present investigation are in line with literature data supporting the effectiveness of a wide spectrum of conservative treatment approaches to myofascial pain of the jaw muscles. Future studies on larger samples over a longer follow-up span are needed on the way to identify tailored treatment strategies.

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Myofascial pain (MP) of jaw muscles is the most common form of temporomandibular disorders (TMD), accounting for up to more than half the patient cases attending TMD clinics throughout the world.[1] Patients with myofascial pain are often compromised from a psychological, as well as a social viewpoint, showing high rates of chronic pain-related disability and depression/somatization scores.[2] Management of MP symptoms is an interesting challenge for clinicians, both at the diagnostic and therapeutic levels,[3] and several treatment approaches have been proposed so far in the literature, ranging from physiotherapy,[4] muscle relaxing drugs,[5] oral appliances,[6] counseling and behavioral therapies,[7] acupuncture,[8] to botulinum toxin injections.[9]

At present, despite claims for conservative approaches,[10] there is no evidence for the most suitable treatment modalities, since there are too few available studies comparing the different approaches. Also, there is a compelling need for the adoption of specific diagnostic

criteria to gather data on treated MP patients, and in order to more easily compare findings from differing research.

One possible strategy to more closely study myofascial pain of the jaw muscles is to look at the treatment options for similar musculoskeletal conditions in other body areas. Among these, physiatric approaches, such as those provided with the Fascial Manipulation techniques (a technique licensed by and registered to Luigi Stecco),[11,12] and botulinum toxin injections,[13] show interesting results for the management of muscle symptoms caused by a number of conditions.

Based on this information, currently available standardized diagnostic guidelines were adopted to recruit patients with myofascial pain of the jaw muscles, and the effectiveness of the two treatment approaches, viz., Fascial Manipulation techniques and botulinum toxin injections, were compared over a three-month period.

Materials and Methods

Thirty consecutive patients (22 females, 8 males, age range 23-69 years) with a Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)[14] diagnosis of myofascial pain, with or without limited opening and bilateral pain lasting for at least six months, were recruited at the TMD Clinic, Department of Maxillofacial Surgery, University of Padova, Italy and randomized to receive either botulinum toxin injections (Group A) or Fascial Manipulation (Group B). At the time of history taking, systemic neurological and/or rheumatological disorders were excluded via a dedicated interview. The concurrent presence of symptoms in the TMJ area (RDC/TMD diagnoses of arthralgia and/or osteoarthritis) was an exclusion criterion. All assessments were performed by the same two trained operators, who were already involved in several previous international research projects providing the use of the RDC/TMD diagnostic guidelines.[15,16] Selected participants were assigned to the study protocols according to a simple one-to-one randomization procedure. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki with the Edinburgh revision and according to current Good Clinical Practice guidelines. Patients gave their written consent to the treatment, and the local ethics committee approved the study.

Protocol A- Botulinum Toxin Injections

Patients included in protocol A underwent a single session of multiple botulin toxin injections in the temporalis and masseter muscles. Injections were performed by the same expert operator using a 0.7 mm 30G needle and with the full respect of current standards for sterility. A total of about 150U of botulinum toxin (Dysport, Ipsen, Ltd., UK) was injected per each treated side. The application technique adopted in the investigation was that described by Paesani, et al.,[17] and by Manfredini and Guarda-Nardini,[18] and already adopted in a previous investigation.[9] Patients were asked to clench the jaws in order to properly identify the muscle to be injected, and then multiple injections were given in the more prominent area of the muscles, with an injection covering, on average, a two cm skin surface over the target muscle tissue. A five-injection minimum with a reverse pyramid pattern was performed in the masseter muscles, and a chess-board pattern was used for the temporalis muscles.

Protocol B – Fascial Manipulation Techniques

Patients included in protocol B underwent a multiple session treatment with Fascial Manipulation.[19] Such a technique provides that a deep digital pressure is exerted over specific Centers of Coordination points defined by the method and selected according to a precise clinical examination, as indicated by Fascial Manipulation guidelines. Therapists use their elbows, knuckles or fingertips to exert pressure on the muscle areas described in **Figure 1**. Each patient underwent three (±1) 50 min sessions of Fascial Manipulation on a weekly basis, for a total of 150 (±50) min over a two- to four-week span. The same trained operator, with more than five years of experience using the technique, performed all manipulation sessions. The choice of the number and specific sites for manipulation was made by the operator on the basis of a tailored analysis of each individual patient's needs, and is reported on **Table 1**.

Outcome Variables and Power Analysis

For each patient, maximum pain levels were assessed on a 10-point VAS scale with 0 being absence of pain and 10 being the worst pain ever. Also, all parameters of jaw range of motion in millimeters (maximum mouth opening, protrusion, right and left laterotrusion) were recorded. All variables were recorded at baseline and at a three-month follow-up. VAS pain levels were also assessed in the immediate post-treatment phases, viz., within one hour of performing either botulinum toxin injection or the last fascial manipulation session. Power analysis based on published literature data on patient populations recruited at the same clinic (20) and assuming a mean VAS value of 6/10 ± 3/10 in the main outcome variable, viz., pain levels, revealed that the study design was able to detect a 50% between-group difference in mean pain VAS values with a 5% risk for type I error, viz., false positive results, and 20% for type II error, viz., false negative results.

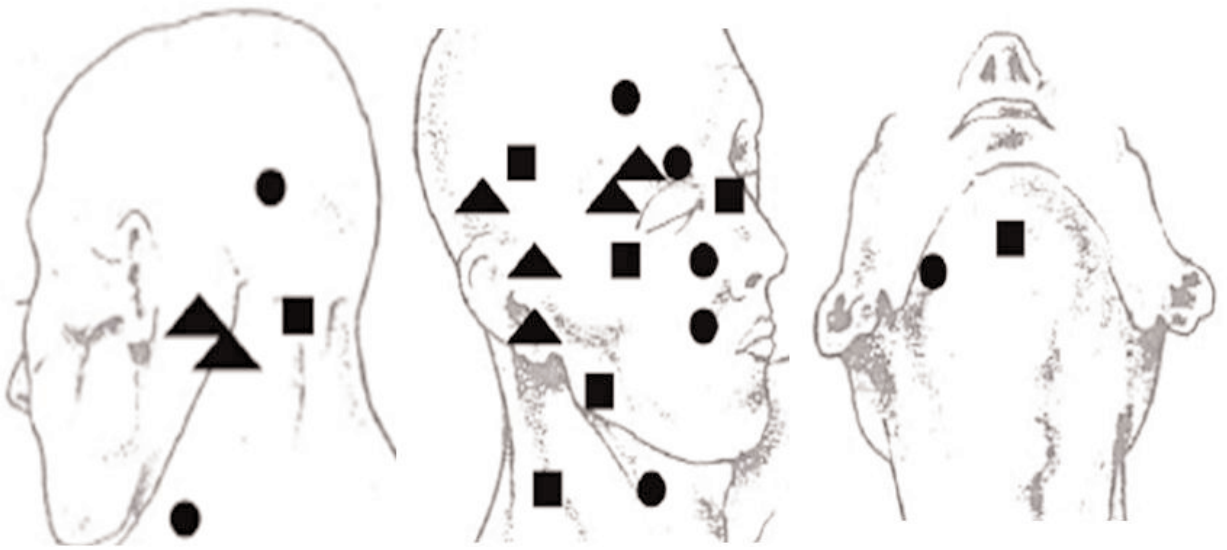

Figure 1
Center of coordination points treated with Fascial Manipulation (a technique licensed by and registered to Luigi Stecco) (■ = frontal plane; ▲ = horizontal plane; ● = sagittal plane).

Table 1
Number of Sites Treated with Fascial Manipulation Per Patient/Session

Patient	Gender	Age	Session 1	Session 2	Session 3	Session 4
BG	M	57	6	4	4	2
BM	F	61	4	4	-	-
CG	F	48	6	4	4	3
DB	F	38	6	4	4	-
FL	F	21	4	4	4	2
GI	F	28	4	4	3	4
GE	F	27	6	4	4	-
LM	F	31	4	5	6	5
MM	M	27	12	6	5	6
RU	M	53	6	4	2	4
RD	M	59	6	6	5	-
SC	F	39	4	4	3	-
SG	F	60	4	4	2	-
ZG	F	53	8	4	4	-
ZL	F	69	4	2	-	-

Statistical Analysis

Changes in the outcome parameters at the end of the follow up period, with respect to baseline values, were tested for significance by means of analysis of variance (ANOVA) for repeated measures. ANOVA was also used to test for the existence of differences between groups as to changes over time in all the outcome variables. Also, ANOVA and Fisher's exact test were performed to investigate respectively for differences in the mean age and to compare gender distribution between groups. For all comparisons, the null hypothesis was that no differences exist between groups as to treatment effects, and statistical significance was set at $p<0.05$.

Results

The two study groups did not differ as to age and gender distribution (**Table 2**). Baseline values in the outcome variables were not significantly different, with the only exception being the right laterotrusive movements.

Table 2
Age and Gender Distribution of the Study Sample

	Female to male ratio	Mean age (SD)
Group A	11:4	47.7 (14.3)
Group B	11:4	43.2 (13.9)

Both treatment protocols provided significant improvement over time as to pain symptoms. VAS pain levels in group A decreased to 5.2 (2.1) at the immediate post-injection assessment and to 4.8 (2.0) at the three-month follow-up, while values in group B were 2.1 (1.4) and 2.5 (2.2) respectively (**Figure 2**). Group A patients showed slight increases in jaw motion parameters (mouth opening 51.4 mm; left laterotrusion 8.7 mm; protrusion 7.0 mm; right laterotrusion 8.7 mm), while values of group B patients remained almost constant over time (mouth opening 52.4 mm; left laterotrusion 9.3 mm; protrusion 6.9 mm; right laterotrusion 9.3 mm). Differences between the two treatment protocols as to changes in the outcome parameters at the three-month follow-up were significant only for laterotrusion movements (**Table 3**).

Discussion

The issue of the treatment of myofascial pain of the jaw muscles is very interesting, since a number of approaches have been proposed over the years and evidence of superiority of one treatment over the others has never been demonstrated. At present, conservative therapies not providing irreversible changes to dental occlusion are considered the best available option due to the high risk-to-benefit ratio.[21] That notwithstanding, many approaches aimed at symptom management are available in the TMD practitioner's armamentarium, and very little data can be drawn from randomized and controlled trials due to their very low number with respect to the broad

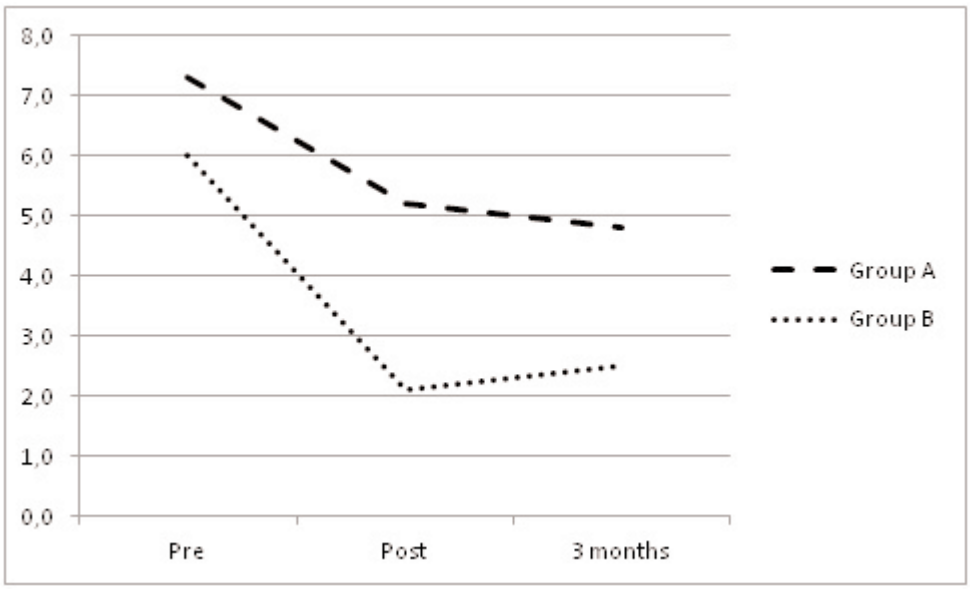

Figure 2
VAS pain levels. Changes over time in the two study groups.

Table 3
Baseline and 3-Month Follow-Up Values for the Outcome Variables
(standard deviations in parentheses)

Outcome measure	Group A baseline	Group B baseline	Expected change sign	Group A (follow-up)	Group B (follow-up)
VAS pain	7.3 (1.1)	6.0 (2.0)	-	-2.5	-3.5
Mouth opening	48.7 (8.3)	52.0 (9.5)	+	+2.7	+0.4
Left laterotrusion	7.3 (3.7)	9.5 (2.8)	+**	+1.4	-0.2
Protrusion	5.8 (3.6)	6.9 (1.8)	+	+1.2	=
Right laterotrusion*	6.9 (3.6)	10.1 (2.3)	+**	+1.8	-0.8

*Significant difference at $p<0.05$ for baseline values
**Significant difference at $p<0.01$ for changes over the 3-month follow-up.

spectrum of literature dedicated to TMD. With this premise in mind, the present investigation compared only two options to manage myofascial pain of the jaw muscles, viz., Fascial Manipulation technique and botulinum toxin injections, since both strategies have been increasingly made use of in recent years in several different musculoskeletal disorders.

The manual therapy, known as Fascial Manipulation, views the myofascial system as a three-dimensional continuum and is based on a comprehensive and functional interpretation of the human facial system. Musculoskeletal dysfunction is considered to occur when the muscular fascia no longer slides, stretches, and adapts correctly. Subsequent adaptive fibroses may develop as a consequence of unremitting non-physiological tension in a fascial segment. The rationale for using the technique is based on the capability of fascial tissues to slide with respect to surrounding tissues thanks to the laxity of collagen fibers.[22,23] The pressure exerted by the therapist over selected specific Center of Coordination points provokes localized hyperemia that may affect the ground substance of the retinacula or the deep fascia, restoring gliding between fibers and allowing a new tensional adaptation throughout the fascial system to re-establish a physiological balance. The technique has a good inter-operator reliability as to the choice of the Center of Coordination points to be treated at the individual level and for the number and length of treatments sessions.[24] Fascial Manipulation has been successfully used to manage signs and symptoms of muscular disorders in several body areas[25-27] and, to the best of the authors' knowledge, this is the first application to the jaw and facial muscles.

Botulinum toxin, a neurotoxin produced by clostridium botulinum in seven different neurotoxic types, causes a prolonged inhibition of neurotransmitter release at peripheral cholinergic nerve terminals at both neuromuscular junctions and autonomic sympathetic and parasympathetic nerve terminals. In recent years, after the discovery of such properties, it was transformed into a widely used drug that is useful for the management of several muscle disorders associated with an excessive cholinergic activity, being adopted as a treatment option for spasticity,[28] blepharospasm,[29] spasmodic dysphonia,[30] and cervical dystonia.[31] Botulinum toxin has also shown good therapeutic effectiveness in the approach to some forms of chronic myofascial pain, even if very little data exists on its use in cervical and maxillofacial conditions.[32] An uncontrolled preliminary investigation by Freund, et al.,[33] found that the injection of 150 units of BTX-A (50U within each masseter and 25U within each temporalis muscle) provided a significant reduction in both objective (mouth opening) and subjective (pain, function, tenderness) jaw function in a sample of 15 subjects with nonhomogeneous temporomandibular disorders over an eight-week period. Similar findings were reported by the same group of researchers in a successive case series study on a larger sample[34] and by Von Lindern,[35] who reported encouraging findings with the injection of 200U of BTX-A per side in a sample of 41 patients with muscular TMD over a six-month span.

At present, the only available randomized clinical trial on the use of botulinum toxin in jaw muscles is the double-blind, placebo controlled investigation with a six-month follow-up period performed by Guarda-Nardini, et al.,[9] which aimed to assess the efficacy of type A botulinum toxin (BTX-A) to treat myofascial pain symptoms and to reduce muscle hyperactivity in bruxers. Twenty subjects with clinical diagnosis of bruxism and with myofascial pain of the masticatory muscles were

randomly enrolled and included either treatment with BTX-A injection or a control group (saline placebo injections). A number of objective and subjective clinical parameters (pain at rest and at chewing; mastication efficiency; maximum non-assisted and assisted mouth opening, protrusive and laterotrusive movements; functional limitation during usual jaw movements; subjective efficacy of the treatment; tolerability of the treatment) were assessed at baseline and at one-week, one-month, and six-month follow-up appointments. Interestingly, improvements in both objective and subjective clinical outcome variables were higher in the botox treated patients than in placebo patients. Also, patients treated with BTX-A referred a higher subjective improvement with time in their perception of treatment efficacy than placebo patients. Accord-ing to the authors, differences were not significant in some cases due to the small sample size. Nonetheless, the findings supported the efficacy of BTX-A in reducing myofascial pain symptoms in bruxers, thus providing pilot data which will have to be confirmed by further research done on larger samples.

In the present investigation, both treatments provided improvement in pain levels, thus confirming that they may be useful in reducing pain symptoms in patients with myofascial pain of the jaw muscles in the short-term. Patients undergoing the cycle of Fascial Manipulation reported slightly higher improvement than subjects treated with botulinum toxin with respect to baseline values. However, between-group differences were not significant, and the interpretation of data is difficult due to the unpaired baseline VAS values. Subjects included in protocol A had significantly higher baseline VAS pain values than those treated with Fascial Manipulation, and the finding that patients of protocol B showed slightly higher improvement is open to a twofold interpretation. First, it might mean that Fascial Manipulation allowed for the achievement of significant positive changes even in the absence of high-intensity pain, and one might expect that changes could have been even more marked in patients with higher VAS levels. Second, it might also mean that randomization of the study sample unfortunately led to the inclusion of patients with worst pain levels, which are likely to be the most difficult to treat, in the botulinum toxin group. Such a problem is inherent with studies on small-sized samples and can be solved only with studies on larger sample groups. Otherwise, studies on the use of botulinum toxin for off-label indications, as in the case of myofascial pain of the jaw muscles, are subject to problems in relation to patient recruitment phases due to ethical and financial issues, and investigations on selected samples are strongly needed in these early stages of botulinum use as a pain medication. In the current investigation, patients were consecutively recruited and fortunately, none of them dropped out, but it is likely that both recruitment and dropouts may become a problem for future studies with larger samples and longer follow-up times. Moreover, the sample size was enough to detect any clinically significant, viz., more than 50%, between-group differences in treatment effect. Thus, despite the nonhomogeneity of baseline VAS values, one could hypothesize that the two treatments were equally effective to treat myofascial pain of the jaw muscles in the short-term.

Patients undergoing Fascial Manipulation showed the highest improvement in the immediate post-treatment assessment, and effects seem to diminish at three months. The course of pain symptoms in patients treated with botulinum toxin showed an opposite trend, with a progressive reduction of VAS values. Such trends may be explained with the different features of the two treatments: one being represented by a single-session few-minute lasting drug injection and the other being performed with a multiple-session 50-minute long manipulation by an operator. The immediate post-treatment effects achieved with Fascial Manipulation are likely to be partly due to some sort of placebo effect due to a positive doctor-patient relationship established during the multi-session manipulation. However, the muscle relaxant effects of botulinum toxin need some weeks to become clinically perceived by the patients.

Data on the jaw range of motion are likely to be of minor interest, because both groups of patients had mouth opening, laterotrusion, and protrusion values within the physiological range. Patients receiving botulinum toxin showed more marked positive changes than those undergoing Fascial Manipulation, but differences seem to be not relevant enough for any clinically-oriented discussion. Interestingly, no relevant side effects were detected in any patients, with the exception of some minor discomfort during chewing reported by the injected patients in the first two-to-three weeks after treatment and of some pain with digital pressure of Center of Coordination points during treatments reported by four patients undergoing Fascial Manipulation. Both effects disappeared and were not rated as relevant by the patients.

This investigation had some limits, the first of which is the relatively short span for follow-up assessment. In any case, the need to gather data on the comparison of different treatments in patients with myofascial pain of the jaw muscles and the difficulties to recruit patients for such a peculiar treatment as botulinum toxin injections justify early presentation of data to minimize the risk of dropouts with successive follow-up assessments. From a methodological viewpoint, a peculiarity of this investigation was

the comparison between two different treatments in terms of number of sessions (single vs. multiple), treatment rationale (muscle relaxant drug vs. Fascial Manipulation), role of the operator (standardized injections vs. tailored manipulation protocols), field of specialty of the main operator (maxillofacial surgeon/TMD practitioner vs. physiatrist). Such differences prevented the authors from achieving the highest quality for randomized controlled trials, because trial blindness of patients and operators could not be guaranteed.

Within these limits, findings from the present investigation are in line with literature data supporting the effectiveness of a wide spectrum of conservative treatment approaches to myofascial pain of the jaw muscles. Increasing amounts of data suggested that physiatric techniques, both active and passive, may be useful to reduce TMD pain symptoms,[36,37] and the same was shown in early investigations on botulinum toxin.[9] It is also possible that a combination of the two treatments could add potential benefit in the clinical setting, as shown by studies on multimodal therapies in TMD patients.[38]

Conclusions

A randomized, controlled trial was performed to compare the effectiveness of botulinum toxin injections and a cycle of Fascial Manipulation (a technique licensed by and registered to Luigi Stecco) sessions in the management of myofascial pain of jaw muscles. Both treatments allowed an improvement with respect to pre-treatment pain levels. In the short-term period, viz., three months, the two treatments seem to be almost equally effective, Fascial Manipulation being slightly superior in reducing subjective pain perception and botulinum toxin injections being slightly superior in increasing jaw range of motion. The gathered data fit well with the currently available literature suggesting that a number of conservative therapeutic approaches may be useful for patients with TMD-related symptoms. Future studies on larger samples over a longer follow-up span are needed in order to identify tailored treatment strategies.

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