

Effect of Botulinum Toxin-A in Myofascial Pain Patients With or Without Functional Disc Displacement

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Purpose: To evaluate the effects of botulinum toxin-A in the treatment of patients who have myofascial pain with or without functional disc displacement.

Patients and Methods: Twenty-four participants were randomly assigned to the study by using Research Diagnostic Criteria for Temporomandibular Disorders. All patients were informed about botulinum toxin-A, and were required to give informed consent. Before the injections, patients were asked to fill out a Biobehavioral Questionnaire to evaluate their pain and psychological status, and afterward, electromyography of the right and left masseter and anterior temporal muscles was recorded. Saline was injected into the masseter and anterior temporal muscles in the placebo group, and botulinum toxin-A was used in the study group. On days 14 and 28, patients were asked to fill out a Biobehavioral Questionnaire again, and electromyography of the right and left masseter and anterior temporal muscles was recorded again.

Results: The study group showed improvement in pain and psychological status. Although a decrease in the action potentials of the masseter muscles on day 14 was followed by an increase on day 28, the reduction of pain scores and improvement in psychological status continued on day 28.

Conclusions: The injection of botulinum toxin-A decreases the muscle action potential in 14 days. The patients also show improvement in pain and psychological status.

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Temporomandibular disorders (TMDs) are subgroups of musculoskeletal and rheumatologic disorders, and

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are considered the major causes of pain in the orofacial region.¹ The most common cause of TMDs is the anterior or medial displacement of the articular disc, which is also known as internal derangement of the temporomandibular joint (TMJ). Displacement of the articular disc can result in decreased joint space; clicking, popping, or crepitation during jaw function; arthritis; condylar resorption; jaw deformities; malocclusion; inflammation; and compression of the bilaminar tissue, all of which can cause various degrees of pain and dysfunction. Chronic disc displacement can lead to deformation of the disc, loss of flexibility, and breakdown of the fibrocartilage covering the condyle and fossa. The disc or, more commonly, the bilaminar tissue posterior to the disc can perforate, and intracapsular adhesions can develop. These changes can lead to a progressive worsening of jaw function and pain. Some common clinical symptoms of TMJ dysfunction include TMJ sounds, TMJ pain, facial pain, headaches, a limited range of mandibular movement, changes in occlusion, masticatory difficulty, earaches, tinnitus, vertigo, and neck, shoulder, and back pain. Some patients with pathologic

internal derangement of the TMJ, however, are asymptomatic or have relatively innocuous clinical symptoms.

Joint noise, pain, and a restricted range of mandibular motion are the most frequent symptoms of TMD.² Generally, treatment focuses on occlusal devices and home care through which the masticatory muscles relax, the load on the joint is relieved, and the adaptation of articular structures is supported.^{3,4} However, in patients with chronic pain, the psychological component of TMD should be considered.

The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) constitute a 2 axis-based statement which is used primarily for research purposes and includes demographics of the study population, patient characteristics, an axis I diagnosis, and an axis II profile. Axis II assesses and classifies the pain condition in terms of pain intensity, pain-related disability, depression, and nonspecific physical symptoms.²

Botulinum toxin-A (BTX-A) prevents the release of acetylcholine in presynaptic terminals of neuromuscular junctions,⁵ and was proposed as an effective treatment for spastic conditions of the head and neck such as oromandibular dystonia and torticollis,⁶ and also in TMD,^{7,8} bruxism,⁹ and hypertrophy of the masseter muscles.¹⁰ However, none of the studies on TMD treatment were randomized, double-blinded, and placebo-controlled.

This study sought to evaluate the effect of BTX-A on pain and the psychological status of myofascial pain patients with or without functional disc displacement, and to compare the effectiveness of BTX-A with a placebo group.

Patients and Methods

This prospective, randomized, double-blinded, placebo-controlled study was planned in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement,¹¹ and was performed by 3 blinded examiners at the Clinics of Temporomandibular Disorders of the Cukurova University Dental Faculty, using RDC/TMD.² The study protocol was approved by the local ethics committee.

Patients with myofascial pain, with or without functional disc displacement, were randomly assigned to the study. They had undergone conservative TMD treatment without complete relief of symptoms. Exclusion criteria were age below 14 years, a history of allergic reactions to BTX-A (Allergan Pharmaceuticals, Ltd, Mayo, Ireland), pregnancy, and lactation. In total, 24 patients were enrolled in the study. Subjects in the study group ($n = 12$) had a mean age of 29.6 ± 12.7 (mean \pm SD) years (range, 16 to 53 years), of whom 10 (83.3%) subjects were female, and 2 (16.7%) were

male. Subjects in the placebo group ($n = 12$) had a mean age of 23.4 ± 4.7 years (range, 20 to 34 years), of whom 10 (83.3%) subjects were female, and 2 (16.7%) were male. Three (25%) patients in the study group and 8 (66.7%) in the placebo group had functional disc displacement and myofascial pain ($P = .1$). Each subject gave informed consent and answered the RDC/TMD Axis II Biobehavioral Questionnaire. The RDC/TMD was translated into Turkish, and the authors² approved its back-translation. It is available on the Web site of the RDC/TMD International Consortium (<http://www.rdc-tmdinternational.org>).

The first examiner, who dealt with randomization and blinding, also prepared the material for injection. The second examiner enrolled subjects according to the study criteria, had the patients fill out the questionnaire, and collected the electromyogram (EMG) records. The injections were made by the third examiner.

Subjects were evaluated at baseline, and on days 14 and 28. They filled out the RDC/TMD Axis II Biobehavioral Questionnaire at baseline, and their EMG records were collected for the right and left masseter and anterior temporal muscles. Then injections were performed. On days 14 and 28, subjects again filled out the RDC/TMD Axis II Biobehavioral Questionnaire, and their EMG records were collected. The intensity of chronic pain, pain-related disability, and levels of depression were measured and evaluated in accordance with the classification described in Axis II of the RDC/TMD.²

Twenty-four envelopes were prepared for randomization and blinding. Twelve envelopes containing papers marked "botulinum toxin A," and 12 envelopes containing papers marked "placebo (control)," were closed tightly, mixed thoroughly, and given numbers from 1 to 24. The envelopes were then opened with each patient allocated blindly to 1 of the 2 study groups. The injection solution was prepared according to what was written on the envelope. If this was "botulinum toxin A," 2 cc of saline were added to the flacon, shaken well to dissolve the powder in accordance with the supplier's recommendations, and placed in an insulin syringe. If this was "placebo (control)," then only 2 cc of saline were placed in the insulin syringe. To prevent bias, both syringes were similar in appearance. Thus, the second and third examiners were unaware of the contents of syringes. The second examiner collected the EMG and questionnaire data, and recorded the date and each subject's name. Subjects filling out the questionnaire were alone in a quiet room, to prevent environmental effects.

An 8-channel surface EMG recorder (WinJaw; Zebri Medizintechnik GmbH, Isny, Germany) was used to record the right and left masseter and anterior

temporal muscles. To determine the points for placing electrodes, subjects were asked to bite down lightly on their teeth for a short time. After palpation of the origin and insertion of the masseter muscle, surface EMG electrodes (Silver/Silverchloride EMG Electrodes, Duo-Trode; Myotronics, Inc, Seattle, WA) were placed parallel to the long axis of the muscle, at equal distance from the origin and insertion of the muscle.¹² The anterior border of the anterior temporal muscle was determined by palpation, and surface EMG electrodes were placed behind the frontal process of zygomatic bone, 1.5 to 2 cm superiorly to the zygomatic arch, perpendicular to the sagittal plane.¹² The patient's skin was cleaned and dried with alcohol before the injections. The subject's head, without any support, was positioned with the Frankfurt horizontal plane parallel to the floor. The EMG records were taken simultaneously from the muscles. Muscle tonus was recorded for 5 seconds at rest position, and then for 5 seconds at maximal clenching. The cycle of rest position and maximal clenching was repeated 3 times during each appointment.

After the collection of data and the removal of electrodes, the third examiner asked the subject if he or she wanted premedication and topical anesthesia before the injection. No patient required premedication or topical anesthesia. If he or she had wanted premedication and topical anesthesia, Midazolam (Dormicum, La Roche, Basel, Switzerland) 0.1 mg/kg and 5% eutectic mixture of Lidocaine and Prilocaine; (Astra Zeneca, Istanbul, Turkey) would have been used.

The masseter muscle is readily accessible clinically. Three diffuse injections were given 1 cm apart along the long axis of the muscle, where the muscle is most active during palpation. Care was taken during injections of this muscle, because diffusion of BTX-A to the zygomaticus major muscle nearby may result in an adverse cosmetic effect, preventing the subject from raising the corner of the mouth and causing an asymmetric smile.¹³

The temporalis muscle is readily accessible superficially in the temple area. It is fan-shaped, and of variable expanse and depth. To weaken this muscle adequately, a superficial injection is considered suitable and no special precautions are required, although advancing the needle too deeply engages the bone and damages the needle.¹³ Two injections were given 1 cm apart, where the muscle is most active during palpation.

Whether the subject's complaint was unilateral or bilateral, injections were given bilaterally. Three points in 2 masseter muscles and 2 points in 2 anterior temporal muscles, for a total of 10 points, were injected with 10 U BTX-A. Subjects were not allowed to use any occlusal appliance, and did not receive any

analgesic, anti-inflammatory, or muscle-relaxing agent during the study.

Statistical analysis was performed with SPSS 15.0 (SPSS Inc, Chicago, IL). The Friedman test was applied to test for changes over the 3 time intervals. Comparisons of 2 time intervals for EMG and score values were performed with the Wilcoxon test. Group comparisons of age and EMG values were performed using the Mann-Whitney test. The χ^2 (Fisher's exact) test was performed for comparisons of categorical data. The *P* values given in Tables 1 to 3 are not adjusted for multiple comparisons.

Results

None of the patients declared that their situation had worsened compared with baseline. No side effects were evident.

EVALUATION OF EMG VALUES

The differences in EMG values at rest position between the study and placebo groups were significant for the left (LMR) and right (RMR) masseter and right temporal (RTR) muscles on day 14 (LMR, $P_{CS} = .002$; RMR, $P_{CS} = .010$; and RTR, $P_{CS} = .001$, where CS refers to the combined study and control groups), but this was not evident at baseline and on day 28 (Table 1). The mean values and standard deviations for the left and right masseter and right and left anterior temporal muscles over time for the placebo groups were 209 \pm 101 mV (day 0), 255 \pm 112 mV (day 14), and 239 \pm 104 mV (day 28); 173 \pm 106 mV (day 0), 258 \pm 114 mV (day 14), and 202 \pm 124 mV (day 28); 175 \pm 105 mV (day 0), 269 \pm 90 mV (day 14), and 205 \pm 120 mV (day 28); and 243 \pm 124 mV (day 0), 227 \pm 135 mV (day 14), and 204 \pm 95 mV (day 28), respectively; and for the study groups, 197 \pm 104 mV (day 0), 115 \pm 66 mV (day 14), and 224 \pm 110 mV (day 28); 197 \pm 105 mV (day 0), 133 \pm 67 mV (day 14), and 220 \pm 122 mV (day 28); 185 \pm 115 mV (day 0), 129 \pm 62 mV (day 14), and 223 \pm 125 mV (day 28); and 246 \pm 75 mV (day 0), 283 \pm 93 mV (day 14), and 194 \pm 69 mV (day 28), respectively. The EMG results for the study group showed a statistically significant decrease over time ($P_t = .046$) and between baseline (day 0) and day 14 ($P_{0-14} = .034$) for the left masseter at rest position, and in the control group, an increase for the RMR over time ($P_t = .076$) (Table 1). No difference was evident in the other EMG variables at rest position.

The differences in EMG values at maximal clenching between the study and placebo groups were significant for all muscles at each time interval (Table 2). The mean values and standard deviations for the left and right masseter and right and left anterior temporal muscles over time for the control groups were 518 \pm

Table 1. CHANGES IN EMG VALUES AT REST POSITION OVER TIME

	Baseline (Day 0) (mV), Mean \pm SD, Median (Minimum/Maximum)	Day 14 (mV), Mean \pm SD, Median (Minimum/Maximum)	Day 28 (mV), Mean \pm SD, Median (Minimum/Maximum)	P_t	P_{0-14}	P_{0-28}
LMR						
C	209 \pm 101 197 (82/319)	255 \pm 112 311 (79/470)	239 \pm 104 294 (42/316)	.717		
S	197 \pm 104 187 (38/317)	115 \pm 66 118 (31/227)	224 \pm 110 290 (27/318)	.046	.034	.433
P_{CS}	.713	.002	.713			
RMR						
C	173 \pm 106 165 (31/315)	258 \pm 114 316 (79/472)	202 \pm 124 243 (26/323)	.076	.034	.388
S	197 \pm 105 183 (25/326)	133 \pm 67 138 (26/225)	220 \pm 122 286 (21/328)	.472		
P_{CS}	.443	.010	.590			
RTR						
C	175 \pm 105 160 (33/318)	269 \pm 90 323 (142/412)	205 \pm 120 237 (42/329)	.013	.019	.433
S	185 \pm 115 151 (34/334)	129 \pm 62 140 (33/222)	223 \pm 125 290 (26/335)	.472		
P_{CS}	.755	.001	.514			
LTR						
C	243 \pm 124 221 (105/472)	227 \pm 135 151 (89/569)	204 \pm 95 175 (70/429)	.717		
S	246 \pm 75 242 (150/375)	283 \pm 93 303 (68/403)	194 \pm 69 159 (129/335)	.050	.308	.050
P_{CS}	.671	.101	.887			

Abbreviations: EMG, electromyogram; LMR, left masseter muscle rest position; RMR, right masseter muscle rest position; RTR, right anterior temporal muscle rest position; LTR, left anterior temporal muscle rest position; C, placebo (control); S, study; t, time; mV, millivolts; P_{CS} , comparison of control and study groups (Mann-Whitney test); P_t , P value for change over time (Friedman test); P_{0-14} , P value for comparison of baseline (day 0) and day 14 (Wilcoxon test); P_{0-28} , P value for comparison of baseline (day 0) and day 28 (Wilcoxon test).

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254 mV (day 0), 500 \pm 243 mV (day 14), and 517 \pm 206 mV (day 28); 507 \pm 238 mV (day 0), 469 \pm 298 mV (day 14), and 499 \pm 223 mV (day 28); 555 \pm 255 mV (day 0), 531 \pm 276 mV (day 14), and 576 \pm 230 mV (day 28); and 537 \pm 170 mV (day 0), 495 \pm 186 mV (day 14), and 571 \pm 220 mV (day 28), respectively; and for the study groups, 301 \pm 227 mV (day 0), 125 \pm 72 mV (day 14), and 234 \pm 102 mV (day 28); 313 \pm 251 mV (day 0), 142 \pm 54 mV (day 14), and 230 \pm 109 mV (day 28); 255 \pm 168 mV (day 0), 219 \pm 159 mV (day 14), and 320 \pm 134 mV (day 28); and 315 \pm 163 mV (day 0), 310 \pm 69 mV (day 14), and 240 \pm 107 mV (day 28), respectively. The EMG values at maximal clenching of the left masseter, RTC, and LTC showed statistically significant differences over time in the study group ($P_t = .046$, $P_t = .028$, and $P_t = .028$, respectively) (Table 2). No difference was found in the placebo groups.

The EMG values at rest position and at maximal clenching of the left and right masseter and anterior temporal muscles at baseline and on days 14 and 28 are given in Tables 1 and 2.

EVALUATION OF BIOBEHAVIORAL QUESTIONNAIRES

The Biobehavioral Questionnaire was evaluated as score changes, as shown in Table 3. Questions 7 to 9 evaluated pain, questions 11 to 13 evaluated disability, and question 20 evaluated psychological status. Comparisons of pain, disability, and psychological status showed no statistical difference over time for the placebo or study groups. Question 20 showed a statistically significant difference for a time point comparison of baseline and day 14 for the control and study groups ($P = .027$ and $.054$, respectively). The Mann-Whitney test for differences in baseline scores between groups was not statistically significant for all question groups in Table 3. Only a borderline significant difference for question 20 on day 14 was observed ($P = .068$).

Discussion

Randomization, blinding, placebo control, and follow-up period have an important effect on the results of a clinical study.¹⁴ In addition, the requirement for

Table 2. CHANGES IN EMG VALUES AT MAXIMAL CLENCHING OVER TIME

	Baseline (Day 0) (mV), Mean \pm SD, Median (Minimum/Maximum)	Day 14 (mV), Mean \pm SD, Median (Minimum/Maximum)	Day 28 (mV), Mean \pm SD, Median (Minimum/Maximum)	P_t	P_{0-14}	P_{0-28}
LMC						
C	518 \pm 254 549 (103/945)	500 \pm 243 490 (113/986)	517 \pm 206 477 (228/833)	.717		
S	301 \pm 227 310 (22/845)	125 \pm 72 119 (33/283)	234 \pm 102 303 (49/318)	.046	.015	.583
P_{CS}	.039	<.001	<.001			
RMC						
C	507 \pm 238 436 (166/938)	469 \pm 298 495 (32/1,100)	499 \pm 223 486 (156/830)	.920		
S	313 \pm 251 283 (22/940)	142 \pm 54 141 (42/228)	230 \pm 109 286 (32/342)	.105	.034	.530
P_{CS}	.045	.007	.003			
RTC						
C	555 \pm 255 629 (99/613)	531 \pm 276 622 (25/808)	576 \pm 230 558 (224/896)	.920		
S	255 \pm 168 291 (30/613)	219 \pm 159 153 (43/502)	320 \pm 134 332 (73/522)	.028	.583	.234
P_{CS}	.005	.006	.007			
LTC						
C	537 \pm 170 508 (268/883)	495 \pm 186 484 (156/792)	571 \pm 220 574 (74/864)	.368		
S	315 \pm 163 260 (150/777)	310 \pm 69 316 (204/423)	240 \pm 107 207 (127/505)	.028	.583	.239
P_{CS}	.001	.007	.001			

Abbreviations: EMG, electromyogram; LMC, left masseter muscle clenching; RMC, right masseter muscle clenching; RTC, right anterior temporal muscle clenching; LTC, left anterior temporal muscle clenching; C, placebo (control); S, study; t, time; mV, millivolts.

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standardized measurements and adequate numbers of subjects prevents bias in terms of examiners and subjects.¹⁴ The present research was a randomized, double-blind, placebo study, and none of the subjects was recorded as lost to follow-up. The differences in measurements of the placebo and study groups clearly indicate that 28 days of follow-up seem adequate. Each examiner always participated in the same part of the study, eg, selecting subjects, data recording, and processing the study material, to prevent any bias. The planning and reporting of the present study was based on the CONSORT statement,¹¹ which was developed for the planning and reporting of randomized, double-blind, placebo-controlled studies.

Although randomization is important in CONSORT-based studies, initial scores of subjects in each group cannot always be equal by means of parameters in CONSORT¹¹ because of the randomization process. Thus, some EMG scores in our placebo group were higher than in our study group (Tables 1-3). LeResche stated that randomization, blinding, control, and adequate follow-up affect the quality of evidence in clinical trials, and this study was in accordance with the considerations of LeResche, except for adequate final sample size.¹⁴

Subjects in the present study were selected from over 500 patients at the Clinics of Temporomandibular Disorders of the Cukurova University Dental Faculty. The selected subjects were first treated with conservative modalities, and no adequate treatment effect was observed. These conservative treatment modalities included reversible occlusal appliances, pharmacologic treatment, physical therapy, and manual treatment.¹⁵ None of these treatments has proved to be wholly or consistently effective, and some are associated with appreciable, undesirable side effects.⁷ Thus BTX-A was used as an alternative to the conservative treatment modalities, and was expected to show therapeutic gains by affecting the muscular component of TMDs.⁷

Because of the paralyzing effect of BTX-A, a decrease was expected in stresses on the TMJ and related tissues, and a reorganization of tissues and a decrease or even elimination of pain was contemplated. This effect is cultivated by preventing acetylcholine release at the motor neurons. As a result of nerve sprouting, muscles were reinnervated, local paralysis was eliminated, and function was restored in 2 to 4 months.⁷ This is the only functional effect of BTX-A. Complications are limited to possible tempo-

Table 3. RESULTS OF BIOBEHAVIORAL QUESTIONNAIRE

Questions	Baseline, Mean \pm SD, Median (Minimum/Maximum)	Day 14, Mean \pm SD, Median (Minimum/Maximum)	Day 28, Mean \pm SD, Median (Minimum/Maximum)	P_t	P_{0-14}	P_{0-28}
7-9						
C	58.9 \pm 14.7 60.0 (26.7/80)	51.1 \pm 20.1 55.0 (23.3/86.7)	51.4 \pm 23.0 55.0 (23.3/80.0)	.255	.346	.978
S	56.1 \pm 17.1 53.3 (33.3/80)	45.8 \pm 18.6 38.3 (23.3/83.3)	43.9 \pm 25.2 31.7 (16.7/96.7)	.129	.209	.323
11-13						
C	31.7 \pm 22.6 26.7 (6.7/93.3)	30.0 \pm 26.8 25.0 (6.7/100)	31.7 \pm 26.3 23.3 (6.7/90.0)	.759	.481	.803
S	30.6 \pm 22.4 26.7 (3.3/66.7)	30.6 \pm 20.4 26.7 (0.0/66.7)	30.3 \pm 20.8 33.3 (0.0/70.0)	.997	.778	.683
20						
C	1.40 \pm 0.76 1.53 (0/2.66)	1.31 \pm 0.63 1.45 (0.22/2.06)	1.40 \pm 0.77 1.56 (0.13/2.50)	.628	.027	.097
S	1.09 \pm 0.44 1.09 (0.66/1.97)	0.87 \pm 0.42 0.97 (0.06/1.34)	0.86 \pm 0.78 0.72 (0.13/2.94)	.290	.054	.076

Abbreviations: $P_{a,b,c}$, within-subject contrast; C, placebo (control); S, study; t, time; mV, millivolts; P_t , P value for change over time (Friedman test); P_{0-14} , P value for comparison of baseline (day 0) and day 14 (Wilcoxon test); P_{0-28} , P value for comparison of baseline (day 0) and day 28 (Wilcoxon test).

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rary regional weakness over the injection sites and an asymmetric smile.

The effect of BTX-A is related to localization and dosage.⁶ Twenty-five to 50 U for the masseter muscles, 5 to 25 U for the temporal muscles, and 5 different injection sites for each muscle were preferred in a previous study.⁷ In the present study, 30 MU for the masseter muscles at 3 injection sites, and 20 MU for the temporal muscles at 2 sites, were injected. Because of an inadequate toxin concentration in the motor endplate, resistance to BTX-A, and faulty preparation or unsuitable storage conditions of BTX-A, problems may be encountered in relaxation of the muscles.⁵

In the present study, surface EMG electrodes were used to evaluate the effect of BTX-A on muscle activity. Surface EMG electrodes are used mainly in kinesthetic analyses of movement disorders, and particularly in differentiating types of tremors, myoclonus, and dystonia; in evaluating gait and posture; and in psychophysical measurements of reaction and movement time.¹⁶ In a previous study, surface electrodes were used to evaluate the muscle relaxation caused by transcutaneous electrical nerve stimulation.¹⁷ Also, parameters such as age, gender, weight, and skeletal type affect the masticatory muscles and head position. These parameters, as well as electrode type and localization of electrodes during data recording, should be investigated in further studies.

No consensus exists about the positions in which EMG activities are minimal. It was reported that the rest position of the mandibula was changed between

0.9 and 3.8 mm from tooth contact.¹⁸ In another study, EMG activity was minimal at 10 mm for the masseter muscle and 12.5 mm for the anterior temporal muscle.¹⁹ Thus, there is no specific vertical dimension at which a minimal EMG record was taken from the elevator muscles. Also, because of differences in patients and muscles, it is hard to declare a specific vertical dimension. Previous studies stated that some portions of the elevator muscles were active at rest position.^{20,21} Surface EMG records of masticatory muscles are used in the diagnosis and treatment of TMDs.²² Although the masseter muscles are multilayered and it is hard to record the muscular activity of superficial and deep fibers, and hard to differentiate anterior digastric muscle activity from mylohyoid muscle activity, a surface EMG is still an acceptable recording method for muscle activity. Regardless of the disadvantages, the popularity of surface EMGs is based on their noninvasive and simple nature. When recording with needle electrodes, hematoma and edema in the muscles, and trauma related to multiple trials, may cause problems in the recording process.

There is no study in the dental literature evaluating the effect of BTX-A on EMG activity in TMD subjects. Therefore, our findings cannot be compared directly with those of previous studies. Nevertheless, different treatment modalities have been evaluated with EMG activity.¹² Landulpho et al¹² evaluated the EMG activity of the masseter and temporal muscles during and after the use of an occlusal appliance, and they reported a significant decrease in EMG activity of the

left and right anterior temporal muscles over time, but the masseter muscles did not present significant differences. These findings are inconsistent with those of our study (Tables 1 and 2). In another study,²³ instead of EMG and RDC/TMD, a visual analog scale (VAS) was used to evaluate the effect of BTX-A on myogenous orofacial pain. It was concluded that BTX-A was not effective or cost-effective, and thus was not recommended as a treatment modality.²³ Botulinum toxin-A is a reversible treatment modality, thus new research should be planned with an increased number of patients.

The existence of asymmetric muscular activity at rest position in the muscles of TMD patients was supported by Holmgren et al²⁴ and Abekura et al.²⁵ Their results demonstrated that the anterior temporal muscle presented statistically different values in electrical activity when the muscles on the right were compared with those on the left. The asymmetric muscular activity between the right and left anterior temporal muscles seen in our study is in concordance with these studies (Tables 1 and 2).^{24,25}

Freund et al⁷ used BTX for TMD treatment, and reported that maximum voluntary clenching begins to decrease after 2 weeks and reverts to baseline levels in 8 weeks. These results, and an absence of a correlation between subjective pain and clenching force,^{7,8} are in agreement with the present study.

The RDC/TMD is a 2 axis-based statement. In Axis I, TMDs are diagnosed, and in Axis II, pain scores and current stress levels are evaluated.^{2,26} All subjects in our study were diagnosed with myofascial pain, with or without functional disc displacement, based on the RDC/TMD (Axis I), and their clinical situations were evaluated by clinical examination and the use of a Biobehavioral Questionnaire (Axis II).

Pain or complaints of pain are subjective, and the declarations of subjects are related to socioeconomic, cultural, and psychological situations. Thus, a clinician who is interested in patients with chronic pain should evaluate the patient from a biopsychosocial perspective. Conti et al²⁷ compared the validity and reliability of a VAS, a numeric scale, and a behavior-rating scale, and reported that the numeric scale was the best way to score reproducible pain. In the present study, questions that involved scoring pain in the Biobehavioral Questionnaire were on a numeric scale. Nixdorf et al used a VAS to determine the effectiveness of BTX-A in chronic myogenous orofacial pain.²³ Although their study was the only one similar to ours in terms of purpose, their conclusions were inconsistent with ours, which may be attributable to the use of a VAS and a lower number of subjects than in the present study.

Pain is the most frequent and complex symptom of TMDs, and is related to the articular and myofascial

structures.¹⁵ However, the source of myofascial pain is not clearly identified.²⁸ In addition, the relationship between myofascial pain and inflammation is not well-understood. There is a consensus that mechanisms of the peripheral and central nervous systems can cause the pain in TMDs.¹⁵ In a previous study,⁷ after the injection of BTX-A to the masseter and temporal muscles, joint capsules were palpated and pain scores were evaluated. It was concluded that the injection of BTX-A decreased the inflammation in the articular structures indirectly.⁷

In evaluations of treatment effectiveness, pain is an important parameter, and has been used in all BTX-A studies.^{8,13,15,29} In these studies, myofascial pain^{13,29,30} and subjective pain⁷ were investigated. Regardless of the source of pain, subjective pain studies^{7,8} have used the RDC/TMD. As in our study, Von Lindern et al³⁰ used BTX-A for eliminating local facial pain and reported an improvement in 91% of their subjects. Other studies using a VAS^{7,8,29} stated that facial and subjective pain in TMD decreased over time, and this is consistent with the decrease on day 14 in our study. Furthermore, this decrease in pain accompanied the decrease in muscle potentials on day 14. Thus it is logical to accept the effectiveness of BTX-A with this time-based correlation.

It should be questioned whether the pain was eliminated by needling or not. However, in view of the consistency between the period without pain and the initiation of the toxin's clinical effect, it may be stated that the source of the effect was the toxin.

In the control and study groups, there was a non-significant improvement in pain scores. There was also significant improvement in the control group, and a nearly significant improvement in the study group, in terms of psychological status. A correlation exists between pain and psychological status. If pain is reduced, a positive change in psychological status is seen, as in this study group.²⁶

In patients with myofascial pain, with or without functional disc displacement, who cannot be treated effectively with conservative modalities, BTX-A can be injected into the masticatory muscles. During the maximal clenching cycle, the masseter muscle action potential is reduced by nearly 80% on day 14, and by 25% on day 28. There were significant differences between pain and psychological status in the placebo and study groups after a follow-up period of 14 and 28 days. Pain and psychological status showed a tendency to improve after BTX-A injections. Although there was a decrease in action potentials on day 14, followed by an increase on day 28, a tendency toward improvements in pain and psychological score was also observed on day 28. Patients with myofascial pain, with or without functional disc displacement, can achieve a positive effect using BTX-A. In conclusion, the sample size in our study may be too small,

but it nonetheless conveys important information about the effectiveness of BTX-A treatment.

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