

## CASE REPORT

# Comprehensive evaluation of botulinum toxin treatment outcomes of a patient with persistent myofascial orofacial pain

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## Abstract

The outcome evaluation method presented in this case study, including Axes I and II findings combined with the results of quantitative bite force and EMG measurements, provides a good tool for proper evaluation of the effect of BoNT-A on patients with myofascial orofacial pain and changes in jaw muscle function.

## KEYWORDS

botulinum toxin, jaw function, pain, temporomandibular disorder

## 1 | INTRODUCTION

Temporomandibular disorders (TMDs) are neuromuscular and musculoskeletal disorders affecting the jaw and muscles of mastication, with myofascial pain being a common condition<sup>1</sup>. The prevailing treatment modalities for myofascial orofacial pain are occlusal splint therapy, pharmacological intervention, behavioral and self-care therapies, and physical therapy<sup>2</sup>. These treatment modalities are usually efficient, but pain symptoms are not always resolved. Injections of botulinum toxin into mastication muscles have recently risen in popularity as a treatment option for patients with refractory pain<sup>3</sup>. However, consensus on its indications is lacking.

Botulinum toxin has received attention in myofascial pain treatment due its muscle relaxation mechanism<sup>4</sup>. However, its analgetic effect is being increasingly emphasized<sup>5-7</sup>. Several studies have shown that botulinum toxin type A (BoNT-A) injections reduce pain in patients with local myalgia as part of TMD<sup>4,8,9</sup>. However, Ernberg et al.<sup>10</sup> reported no significant difference in pain reduction between BoNT-A and placebo, and some studies have failed to show that BoNT-A is more effective than conservative treatment modalities<sup>3,7</sup>. Contradictory results support the multifaceted nature of TMD, and there is still a place for controlled studies regarding the effectiveness of BoNT-A in myofascial pain where the etiological factors and treatment outcomes are comprehensively assessed. Due to the

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paralytic effect of BoNT-A on muscles, it is also important to evaluate the physiological changes in muscle activity. Since some adverse effects, such as bone volume changes of the mandible, have been described, the duration of the paralytic effect is an important issue, especially when considering repeated injections<sup>11,12</sup>.

The outcome evaluation method presented in this case, including Axis I and Axis II findings, provides a good tool for proper evaluation of the effect of BoNT-A in patients with myofascial orofacial pain. Objective measurable parameters, such as electromyography (EMG) and bite force measurements, were also applied in this case study to follow the changes in jaw muscle function.

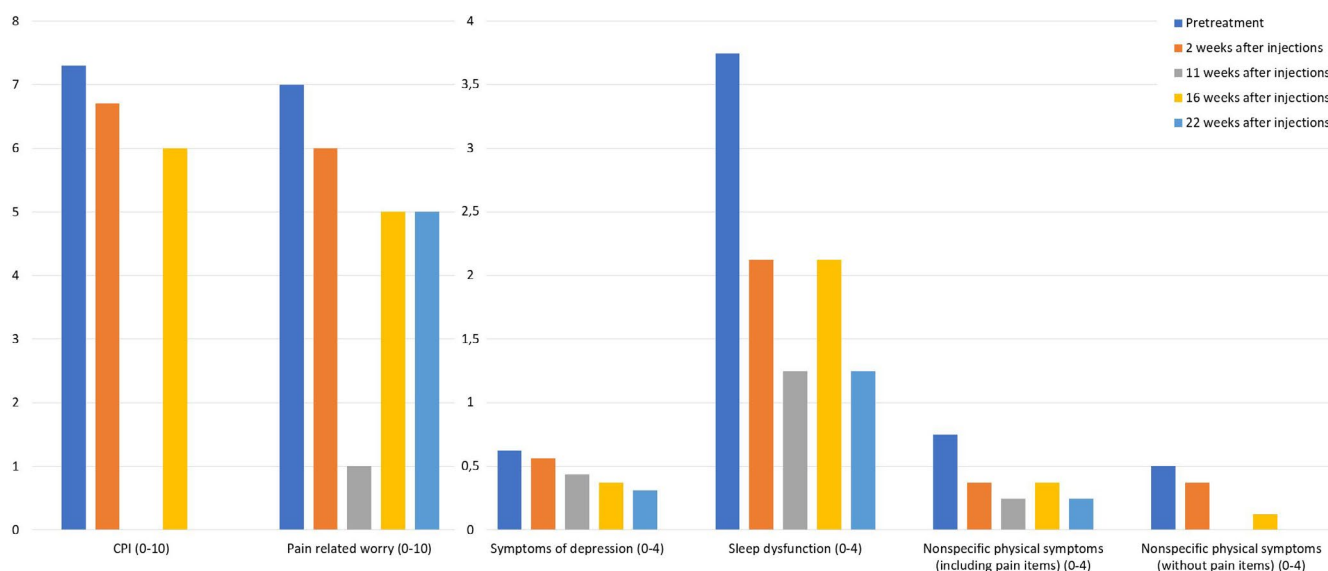
## 2 | CASE HISTORY AND EXAMINATION

The patient is a 53-year-old woman whose symptoms have lasted for over 30 years and with pain that is troublesome 1–3 times per month. She sought treatment for facial pain, headache, and self-reported awake bruxism. The patient had no systemic diseases, no medication, and did not smoke. She noted that symptoms correlated often with stress episodes. The patient was treated with many different TMD treatment modalities, such as splint therapy, non-steroidal anti-inflammatory drugs, and a soft food diet, with poor success.

The clinical examination revealed a maximum mandibular opening of 50 mm and a normal range of eccentric movements. Joint pain or sound was not detected. There was a stable occlusal condition in a musculoskeletal stable position. According to the pain drawing, the pain that the

patient experienced during the last six months was intra-oral and in all areas of the head, neck, face, and shoulders. Palpation of the muscles of mastication revealed muscle tenderness in the areas of the masseter and temporalis with no referred pain. Palpation-induced pain was familiar to the patient. She also reported clenching of the jaw during the day and the jaw being stiff. Since the pain symptoms had lasted for years and conservative treatments of muscle pain were ineffective, activity within the central nervous system (CNS) was speculated to be involved in the pain input. Clinical diagnosis was based on the standardized clinical examination protocol and Axis I decision tree of the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)<sup>13</sup>. The diagnosis was chronic frequent primary myofascial orofacial pain without pain referral<sup>14</sup>. One of the etiological factors was parafunctional muscle activity (awake bruxism) and stress-related muscle co-contraction. In this study, we decided to try BoNT-A injections as a treatment option combined with comprehensive assessments of treatment outcome and objective evaluation of muscle activity.

The Characteristic Pain Intensity (CPI) score was calculated on a 0–10 scale to determine current, worst, and average pain intensity during the past six months. Before the treatment, the score was 7.3. The chronic pain grade (CPG, baseline to six months, grades 0–IV) was II, corresponding to “High-intensity pain, without disability.” Jaw functional limitations were observed in the following activities: chewing tough food, smiling, yawning, and tooth brushing. The degree of pain-related worry was 7 (0–10 scale). Based on the Symptoms Checklist-90 Revised (SCL-90R) questionnaire, the patient had only mild symptoms of depression, with an average score of



**FIGURE 1** A histogram of RDC/TMD Axis II findings before BoNT-A injections and at each follow-up visit at 2, 11, 16, and 22 weeks after treatment. The following parameters are shown: Characteristic Pain Intensity (CPI), Pain-related worry, Symptoms of depression, Sleep dysfunction, Non-specific physical symptoms (including pain items), and Non-specific clinical symptoms (without pain items)

0.5 (0–4 scale) (Figure 1). The same questionnaire revealed a severe sleep disorder, with an average score of 3.0 (0–4 scale). The average score of non-specific physical symptoms with pain items was 0.6 and non-specific physical symptoms without pain items 0.4 (0–4 scale). The initial average electromyography (AEMG) value of the masseter muscle during clenching with a maximum force was 241 mV and at rest 45 mV, and the average maximum bite force was 580 N (Figure 2). Axis II biopsychosocial assessment instruments of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) were used to evaluate the effect of treatment on disability and psychological status<sup>15</sup>.

The following questionnaires were used before the treatment and at each follow-up visit:

Axis I (Physical findings).

- Demographics
- Clinical examination form (DC/TMD)

Axis II (Disability & Psychological Status).

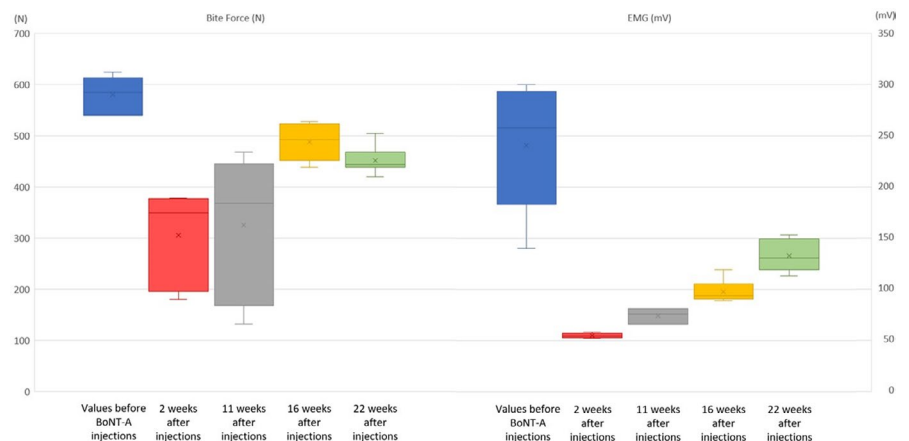
- Pain Drawing
  - a. None: number of body areas with pain =0
  - b. Mild: number of body areas with pain =1
  - c. Moderate: number of body areas with pain =2
  - d. Severe: number of body areas with pain =3
- Graded Chronic Pain Scale (GCPS) 1.0
  - a. 0: no TMD pain in the preceding six months
  - b. I: low disability, low pain intensity
  - c. II: low disability, high pain intensity
  - d. III: high disability, moderately limiting
  - e. IV: high disability, severely limiting
- GCPS 1.0 grades are derived from seven questions measuring
  - a. Characteristic pain intensity (CPI) (current, worst, average) (range 0–10; 0 = no pain, 10 = worst pain)

- b. Disability days
  - c. Pain-related interference with daily, social, and work-related activities
- Questionnaire for measuring jaw functional limitation (11 items with *yes* or *no* option: chewing, drinking, exercising, eating hard foods, eating soft foods, smiling/laughing, sexual activity, cleaning teeth or face, yawning, talking, having your usual facial appearance)
  - Pain-related worry (range 0–10; 0 = not at all worried, 10 = extremely worried)
  - Ability to control pain (range 0–6) or the ability to decrease pain (range 0–6)
  - RDC/TMD\_FIN Depression and Somatization Scores based on the Symptom Checklist 90, Revised (SCL-90R) (5-point Likert scale: 0 = not at all, 4 = very much), including the following assessments:
    - Symptoms of depression (20 questions)
    - Sleep dysfunction (3 questions)
    - Non-specific physical symptoms (including pain items) (12 questions)
    - Non-specific physical symptoms (without pain items) (7 questions)

EMG of masseter muscle and bite forces were assessed before the treatment and after the BoNT-A injections at each follow-up visit<sup>16,17</sup>. A series of recordings consisted of an exercise lasting 60 seconds so that every 10th second the patient was asked to bite hard for 5 seconds, followed by a 5-second relaxation. The values of AEMG were selected from the middle of each 5-second relaxation and clench periods. Maximum bite force was selected from each clench period. Six values of AEMG and bite force were selected at each patient's visit, and the average values were calculated.

The patient received a one-time treatment of 50 units of BoNT-A (Xeomin®, supplied by Merz Pharmaceuticals GmbH, Germany); 2/3 of the dose was injected into the bilateral masseter muscles (16.7 units each masseter) and 1/3 into the bilateral temporalis (8.3 units each temporalis).

**FIGURE 2** Box plots of the average electromyography (EMG) and bite force values. The measurements were done before the BoNT-A injections into the masseter and temporalis muscles (blue) and at 2 weeks (red), 11 weeks (gray), 16 weeks (yellow), and 22 weeks (green) after the injections. Each box plot shows median (solid line inside the box), mean (cross inside the box), and 25th and 75th percentiles



Three injections located a distance of 1–1.5 cm apart were applied along the inferior border of the masseter, and two injections located a distance of 2 cm apart were applied along the anterior part of the temporalis<sup>8,12</sup>. Before the injections, the posterior and anterior edges of the m. masseter were marked as was the ear lobe—mouth corner line to ensure a safe distance from the parotid duct and m. risorius (Figure 3). The patient was asked to clench in order to properly identify the muscles. Follow-ups were performed at 2, 11, 16, and 22 weeks after the BoNT-A injections.

At two weeks after the injections, there were no significant changes in pain location, pain intensity, or degree of disability, with chronic pain grade remaining at II and CPI at 6.7. However, functional limitations were no longer observed. The score for pain-related worry was 6 (range 0–10). The following scores were obtained from the Axis II biobehavioral questionnaire (range 0–4): symptoms of depression 0.45, sleep dysfunction 1.7, and non-specific physical symptoms with and without pain items 0.3 (Figure 1). The AEMG value during clenching with maximum force dropped to 55 mV and the average maximum bite force to 305 N (Figure 2). No changes occurred at AEMG rest (45 mV).

At 11 weeks after the injections, only the parietal region remained as a pain area. The chronic pain grade was 0, meaning that TMD pain and its related disability were no longer present. No functional limitations were observed. Pain-related worry was 1 (range 0–10). The following scores were obtained from the Axis II biobehavioral questionnaire (range 0–4): symptoms of depression 0.35, sleep dysfunction

1.0, and non-specific physical symptoms with pain items 0.2 and without pain items 0 (Figure 1). The AEMG value during clenching with maximum force was 74 mV, and the average maximum bite force was 326 N (Figure 2).

At 16 weeks after the injections, the pain distribution level was moderate with two areas affected: the temporalis and the right side of the neck. The severity of chronic pain was graded as II, and CPI was 6.0. Nonetheless, no functional limitations were observed. Pain-related worry was 5 (range 0–10). The following scores were obtained from the Axis II biobehavioral questionnaire (range 0–4): symptoms of depression 0.3, sleep dysfunction 1.7, and non-specific physical symptoms with pain items 0.3 and without pain items 0.1 (Figure 1). The AEMG value during clenching with maximum force was 98 mV, and the average maximum bite force was 488 N (Figure 2).

At 22 weeks after the injections, the pain distribution level was still moderate, affecting the parietal and temporal regions. CPI score was 0, with no functional limitations. Pain-related worry was 5 (range 0–10). The following scores were obtained from the Axis II biobehavioral questionnaire (range 0–4): symptoms of depression 0.25, sleep dysfunction 1.0, and non-specific physical symptoms with pain items 0.2 and without pain items 0 (Figure 1). The AEMG value during clenching with maximum force was 133 mV, and the average maximum bite force was 452 N, indicating that the physiological effect of BoNT-A was still present (Figure 2).

## 2.1 | Ethics approval

The study adhered to the tenets of the Declaration of Helsinki, and the regional Ethics Review Board of Helsinki University Hospital approved the study protocol (ID: HUS/3167/2018).

## 3 | DISCUSSION

Several studies have shown the efficacy of BoNT-A in treatment of TMD-related myofascial pain<sup>4,7,8</sup>. The use of BoNT-A is increasing; however, consensus on its indications, dosage, and injection sites is lacking. Different types and doses of botulinum toxin used in research complicate comparison of results, as do variations in the outcomes measured and the timing and duration of follow-ups<sup>9</sup>. The only clinical trial where different doses were compared did not show a benefit with larger doses of BoNT-A<sup>7</sup>. In this study, a beneficial effect regarding subjective findings was achieved with 50 U of BoNT-A. Other studies with the doses used in this case—16.7 units for each masseter and 8.3 units for each temporalis—have not been reported in the literature in relation to myofascial pain. Pain assessment

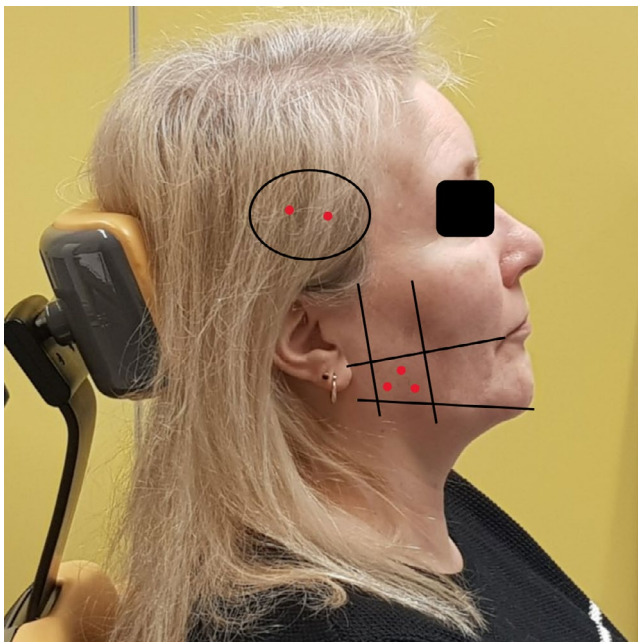


FIGURE 3 Injection sites of BoNT-A in masticatory muscles: 3 sites for M. masseter and 2 sites for M. temporalis



tools revealed that with this dose the pain symptoms of a 53-year-old woman were relieved for at least 22 weeks, with the best therapeutic gain achieved at 11 weeks. Before the injections and two weeks after, the chronic pain grade was II, corresponding to “high-intensity pain, without disability,” and at the 11-week follow-up the score was 0, corresponding to “no TMD pain.” The chronic pain grade reflected “high-intensity pain, without disability” at the 16-week follow-up and then diminished to 0 (“no TMD pain”) at the 22-week follow-up, which can be explained by the natural course of recovery. In addition, the improvement of symptoms during the first follow-ups can partially be explained by natural recovery as well as the placebo effect<sup>10</sup>.

The reduction in TMD pain level correlated with a decrease in sleep dysfunction level and an improvement in jaw function. Pain-related worry diminished and improvements in psychological factors were observed. Non-specific physical symptoms (including pain items) decreased from “moderate” (0.6) to “normal” (<0.5). Other SCL-90-R findings were classified as “normal” throughout the research. Initially, low Axis II scores, as in this patient, predict treatment success<sup>18</sup>.

The increased level of muscle activity as one of the etiological factors in this case might support the beneficial effect of the BoNT-A treatment since muscle relaxation was achieved. However, clenching is not likely to be the cause of the chronic pain conditions<sup>19</sup>. Due to the fact that the pain had been bothersome for the patient for years and that CNS was exposed to prolonged nociceptive input, the beneficial effect of BoNT-A is better explained by its effect on nociceptive neurotransmitters. There is evidence that BoNT-A attenuates pain independently of its paralytic effect at both peripheral and central levels<sup>3,20</sup>. This mechanism of action is also emphasized in the treatment of orofacial myofascial pain<sup>7</sup>.

The reduced EMG values of the masseter muscle after BoNT-A injections clearly show the physiological effect of the drug. In this case, before the injections, the AEMG was 241 mV and two weeks later the value had dropped to 55 mV, which was only slightly higher than the AEMG value at rest (45 mV) (Figure 1). A considerable reduction in muscle activity was observed throughout the study, that is, up to 22 weeks. Decreased bite forces were also observed; the mean value obtained before treatment was 580 N, and after the injections the lowest values were seen at 2 weeks (305 N) and 11 weeks (326 N) (Figure 1). Bite forces reflect masticatory function but with a lower sensitivity, and patient-related factors might affect these values.

In this case study, the patient did not experience any clinically significant adverse effects for 22 months. The temporary side effects reported in the literature are localized pain, difficulty chewing, and focal muscle weakness<sup>9</sup>. A decrease in mandibular bone volume in the areas of the

mandible angle, alveolar process, and condyle in response to decreased mechanical loading has also been reported<sup>7,11,12</sup>. These changes might lead to clinical consequences such as deterioration of jaw function due to condylar degeneration<sup>21</sup>. According to some studies, bony changes are still present 12 months after the injections<sup>12,22</sup>. Bone remodeling in response to mechanical loading is a continuous process, meaning that bone changes are also reversible<sup>23</sup>. EMG measurements are a reliable, convenient, and safe method to follow changes in muscle activity, and decreased values may predict the presence of latent adverse effects beyond the injected muscle<sup>16</sup>. To date, only one study has been published in which EMG parameters were evaluated over a follow-up of 180 days<sup>7</sup>. In that study, the decreased muscle activity was still present at 180 days with doses of 140 U and 200 U of BoNT-A, and total recovery of activity was observed with a dose of 80 U of BoNT-A. We showed that muscle activity was still reduced at the 22-week follow-up with a dose of 50 U. Further trials with moderate doses of BoNT-A and a longer follow-up period combined with muscle activity assessment are needed to better interpret the use of BoNT-A in myofascial orofacial pain treatment.

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## CONFLICT OF INTEREST

The authors do not have any financial relationships that might lead to a conflict of interest.

## AUTHOR CONTRIBUTIONS

VS: contributed to manuscript writing and performed the material preparation. AK: was responsible for the construction of the manuscript. PK: contributed to the study conception and design and the diagnosis and examination of the patient. OT: contributed to the study conception and design. All authors were involved in the editing and final approval of the manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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