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Clinical Paper
TMJ Disorders

Clinical outcomes of Botox injections for chronic temporomandibular disorders: do we understand how Botox works on muscle, pain, and the brain?

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Abstract. The main objective of this retrospective review was to analyze the clinical outcomes following the use of botulinum toxin (onabotulinumtoxinA, Botox) injections to relieve the symptoms of chronic temporomandibular disorders (TMD). Seventy-one patients with a diagnosis of TMD (according to the RDC/TMD international consortium) associated with or without bruxism and refractory to conventional treatment (e.g. oral appliances, physiotherapy, etc.) received Botox injections into the temporalis and masseter muscles. Subjective responses to Botox were categorized as 'beneficial' or 'not beneficial', as patient-reported outcomes based on the subjective reduction in pain and/or improvement in function. Fifty-five of the 71 subjects (77%) reported beneficial effects with Botox. Subjects with a concomitant bruxism diagnosis reported significant improvement over subjects without bruxism (87% vs. 67%; $P = 0.042$). Subjects with stress-related psychiatric comorbidities and bruxism had a significantly higher benefit than those with stress-related psychiatric comorbidities alone ($P = 0.027$). Patients reported less improvement if the time between the initial Botox injection and follow-up was less than an average of 5 weeks, compared to an average follow-up of 5–10 weeks ($P = 0.009$). The subgroup TMD diagnosis and time interval post-injection are important predictors of patient-reported beneficial outcomes.

Key words: temporomandibular joint; Botox; chronic pain; bruxism; post-traumatic stress disorder; anxiety.

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During the second part of the 1990s, botulinum toxin injections (onabotulinumtoxinA, Botox) were introduced as a treatment for temporomandibular disorders (TMD).[1] At that time, it was appreciated that patients with acute, subacute, or chronic TMD pain derived relief from this novel approach. This was encouraging because similar to many other chronic functional pain syndromes,[2–5] TMD has the potential to become centralized, leading to symptoms that are beyond the control of traditional interventions. Overall, our lack of understanding of the centralization process has contributed to a deficit of effective treatments that are available for chronic pain patients; this can result in severe debilitation and have significant negative effects on various measures of quality of life for those individuals suffering with chronic pain.[6,7] The current approaches and treatment responses for TMD problems in general are quite different,[8,9] especially if therapeutic effects are considered for acute versus chronic pain. Thus, it is imperative to identify new therapeutic strategies to treat both the acute and chronic TMD pain patient.[10] Fortunately, Botox injections may play a valuable role in such a desired treatment approach.

It is commonly understood that Botox exerts a therapeutic effect through well-described molecular actions at the neuromuscular junction. A local paralytic effect is produced via inhibition of acetylcholine release,[11] and this synaptic blockade has been taken advantage of to successfully treat a wide number of clinical problems, including movement disorders,[12] focal hyperhidrosis,[13] rhytids,[14] urological pain syndromes,[3] and migraines.[15] Utilizing Botox to treat both acute and chronic centralized TMD pain is a logical extension of its clinical usefulness,[16–18] although the exact mechanisms of how this might occur have yet to be completely elucidated.[19]

The objective of this study was to analyze the retrospective clinical outcomes following the use of onabotulinumtoxinA (Botox) to relieve the symptoms of chronic TMD. In addition, attention is called to open questions regarding the timing, duration, and location of action of therapeutic Botox injections.

Materials and methods

Subjects

US military veterans treated at the TMD clinic of the San Francisco Veterans Affairs Health Care System, San Francisco (SFVA) between 2002 and 2013 were included in this study. The diagnosis of TMD was made in accordance with the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD). Subject data were obtained from the computerized patient record system (CPRS) from consecutive standardized encounters for each patient. From an initial group of 151 patients treated for TMD problems, 71 patients without any benefit from conventional treatment (psychological support, splint therapy, physiotherapeutic support) after 6 weeks were included in the study. Their demographic characteristics are shown in Table 1.

Table 1. Descriptive characteristics of the population treated with Botox injections ($N = 71$).

Characteristics	
Sex, *n* (%)	
Male	46 (64.8)
Female	25 (35.2)
Age, years, mean ± SD (range)	45.8 ± 13.2 (25–80)
Age, years, *n* (%)	
20–29	9 (12.7)
30–39	15 (21.1)
40–49	16 (22.5)
50–59	20 (28.2)
60–69	8 (11.3)
70–79	2 (2.8)
80–89	1 (1.4)
Comorbidities, *n* (%)	
Bruxism	38 (53.5)
Stress-related psychiatric comorbidities	37 (52.1)
Fibromyalgia	10 (14.1)
DJD other than TMJ	29 (40.8)
DJD other than TMJ + fibromyalgia	5 (7.0)
Presenting symptoms, *n* (%)	
Joint pain only	7 (9.9)
Myofascial pain only, including those presenting with temporal headache	27 (38.0)
Joint pain + myofascial pain	37 (52.1)

SD, standard deviation; DJD, degenerative joint disease; TMJ, temporomandibular joint.

It was also determined whether or not there was a history of (1) a previously established stress-related psychiatric diagnosis, as noted in the medical record; (2) masticatory muscle fibromyalgia for more than 6 months, as noted in the medical record; (3) bruxism, by patient self-report and clinical examination.

Subjective responses to Botox (Allergan Inc., Dublin, Ireland) were categorized as 'beneficial' or 'not beneficial', based on a documented reduction in pain and/or improvement in function, as a patient-reported outcome after 5 and 10 weeks of post-treatment follow-up. No adverse events after Botox injections were recorded in the patient electronic health records. No patient dropouts were recorded. Responses were measured for statistical significance using a χ^2 test ($P < 0.05$ deemed significant). The Institutional Review Board approved this retrospective clinical review and specified that there be no contact with the subjects; however, informed consent was obtained from each subject who received Botox treatment. Adverse events were monitored and included: evidence of distant or contiguous spread of Botox, systemic effects such as difficulty with respiration, injection site discomfort or infection, and allergic reaction.

Intervention

All subjects received a one-time treatment with a total of 100 units of Botox, which was reconstituted with sterile saline (100 units/4 ml of sterile saline). The Botox was injected into the bilateral temporalis and masseter muscles. Three points were injected along the inferior portion of the masseter and two points along the anterior–superior portion of the temporalis. Ten units of Botox were delivered to each point using a 5-ml syringe and a 30-gauge needle. The injection technique involved inserting the needle into the soft tissue until bone was encountered and then the needle was withdrawn approximately 2–4 mm so that the tip was in the muscle, at which time the liquid was injected.

Statistical analysis

Subjective responses to Botox were identified by a review of the medical records and categorized as beneficial or not beneficial as a patient-reported outcome. A

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