Long-term efficacy of onabotulinum toxin in treating persistent myofascial pain and masticatory muscles hypertone in an adolescent with bruxism. A 7-year follow-up case report

M. Storari[1], M. Aprile[1], S. Mameli[1], G. Denotti[3], D. Viscuso[1]

[1]*Department of Surgical Science, College of Dentistry, Orofacial Pain Centre, University of Cagliari, Cagliari, Italy*
[2]*Pain Therapy Unit, Businco Hospital, ASL 8, Cagliari, Italy*
[3]*Department of Surgical Science, College of Dentistry, Director post-graduate program in Paediatric Dentistry, University of Cagliari, Cagliari, Italy*

E-mail: m.storari93@gmail.com

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Abstract

Background Temporomandibular disorders (TMDs) represent a common chronic complaint, which includes myofascial pain (MP). Although several therapeutical options have been proposed to control bruxism-related muscle hyperactivity, there is not enough evidence to define a standard approach. The present article describes the case of a 14-year old male patient with a history of painful mandibular close lock.

Case report The patient was diagnosed with persistent myofascial pain in the left masseter, bilateral disc displacement with reduction, and retrodiscitis and capsulitis in the left temporomandibular joint. Awake and sleep bruxism were also present. Since first line treatments failed in managing the disorders, injections of onabotulinum toxin (BoNT-A) were performed. After one month the pain decreased significantly and the jaw movements were restored. The patient was recommended to avoid hard and/or rubbery food, wide movements of the jaws and teeth clenching and to wear orthodontic appliance during the night since the joint damage was moderate. We report the 7-year follow-up demonstrating the long-term efficacy of a single injection of onabotulinum toxin in masseters and temporalis muscles in order to treat masticatory pain and dysfunctions.

Conclusion The authors suggest that BoNT-A could be an optimum treatment for persistent MP and bruxism in young adolescents when first-line therapies fail.

KEYWORDS Bruxism, Masticatory muscles hypertone, Myofascial pain, Onabotulinum toxin.

Introduction

Temporomandibular disorders (TMDs) are a significant public health concern affecting around 5% to 12% of the population [National Institute of Dental and Craniofacial Research, 2018]. Among subjects with TMDs, Myofascial Pain (MP) represents a common chronic complaint with a prevalence up to 48% [Manfredini, 2011]. Signs and symptoms may vary from mild discomfort to severe pain and dysfunctions leading to disabling consequences affecting patients' quality of life [Celiker, 2010; Dugashvili G, 2019]. The aetiology of MP is complex and unfortunately not well understood [Ohrbach, 2016]. It represents a complex disorder within a biopsychosocial illness model. Trauma, fatigue, hypovitaminosis, infections and poor physical conditions, as well as stress and deep pain input, were firstly described as related factors [Simons, 1999; Okeson, 2014]. Nevertheless, when local symptoms persist beyond the time of healing, new peripheral and central processes guide the evolution to chronic pain [Wall, 1979]. Bruxism is reported to contribute to MP [Sierwald, 2015; Manfredini, 2003], despite the relationship between bruxism and TMDs is still unclear [Manfredini, 2020]. Bruxism not necessarily represents a treatment demanding condition *per se* and should be only considered a repetitive masticatory muscle behavior which can be harmless, harmful or even protective, depending on other clinical conditions [Manfredini, 2020].

Although several therapeutical options have been proposed to control bruxism-related muscle hyperactivity, yet there is not enough evidence to define a standard approach [Manfredini, 2020]. Similarly, since the pathogenesis of MP is not clearly defined, conservative and reversible therapies are recommended [Greene, 2001]. Drugs [Dym, 2016], oral appliances (OAs) such as bite [Conti, 2012], counselling and physiotherapy [Conti, 2012; De Laat, 2013] are the most suitable therapies. Onabotulinum toxin (BoNT) may represent a promising alternative to traditional therapies. BoNT is an exotoxin produced by the spore-forming anaerobic Gram-positive bacterium Clostridium botulinum, known to cause potentially fatal food poisoning. Since the late 1980s, the US Food and Drug Administration (FDA) has approved Type-A BoNT (BoNT-A) for the treatment of numerous muscular disorders [Thenganatt, 2012]. Similarly to the paralytic effect in cholinergic neuromuscular junctions, growing evidences support that BoNT-A exerts pain reduction by blocking peripheral neurotransmitters' release from sensory nerves

FIG. 1 Maximum not forced mouth opening before (left) and 7 years after BoNT injection (right).

[Matak, 2014; Cherington, 2004]. Thus, albeit no clear consensus exists regarding its use in treating TMDs [Ernberg, 2011; Patel, 2020; Kurtoglu, 2008; Guarda-Nardini, 2012], BoNT-A has been introduced as a potential approach for controlling bruxism in patients with persistent MP of masticatory muscles (MMs) [Hosgor, 2020; Guarda-Nardini, 2008]. In the present work, we describe the long-term efficacy of BoNT-A in treating persistent MP symptoms in a 14-year-old patient with bruxism.

Case report

A 14-year-old male student was referred by his dentist to the Orofacial Pain Center at the Dental Clinic of the University of Cagliari, Italy, in February 2015, with severe pain on the left side of the face. The patient reported that symptoms had started 2 years before without any apparent cause. No history of trauma, headaches and other relevant diseases was referred. On the other side, a positive anamnesis emerged regarding both awake and sleep bruxism. Pain typically occurred in the morning, was exacerbated by jaws' function and subsided with rest. Chewing, clenching and grinding of the teeth, biting the lips and/or cheeks, and wide opening of the mouth were described by the patient as the most common triggers of the pain. Pain usually lasted less than a minute reaching a peak of around 8 points on a 10-mm visual analog scale (VAS) (with 0 being absence of pain and 10 being the worst pain ever experienced). During the last year the patient reported a chronic limitation of jaw opening with two episodes of painful open lock of the mouth. Additionally, the patient reported a severe reduction of the quality of life and poor school performances.

At the clinical examination the patient showed a maximum mouth opening of 28 mm (Fig. 1), increasing up to 31 mm with forced assistance. The right and left lateral excursions were 5 mm and 2 mm, respectively, and the mandible slightly deviated 2 mm on the left side during mouth opening. The median line was 2 mm deviated to the right side. Noises during movements were appreciated in both joints while tenderness under palpation, both external and internal, was referred only on the left temporomandibular joint (TMJ). Palpation of the MMs provoked pain in the left masseter and revealed contracture and hypertonia of the same muscle. The patient was firstly educated to control bad and parafunctional habits and to apply a heat pack on masseters before bedtime for 20 minutes. The patients was recommended to avoid hard and/or rubbery food, wide movements of the jaws and teeth clenching during the day.

After 1 month the patient underwent Magnetic Resonance (MR) which showed a reduced joint space and anterior

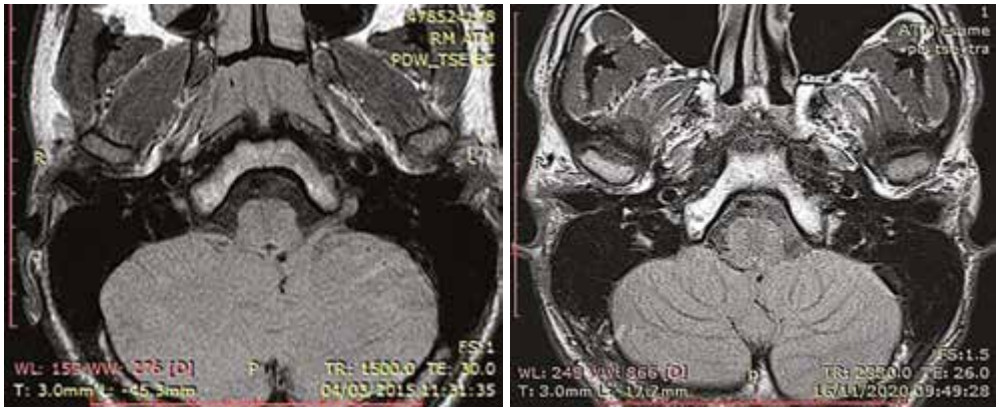

FIG. 2 Transversal section MRI. March 2015 (left) and November 2020 (right).

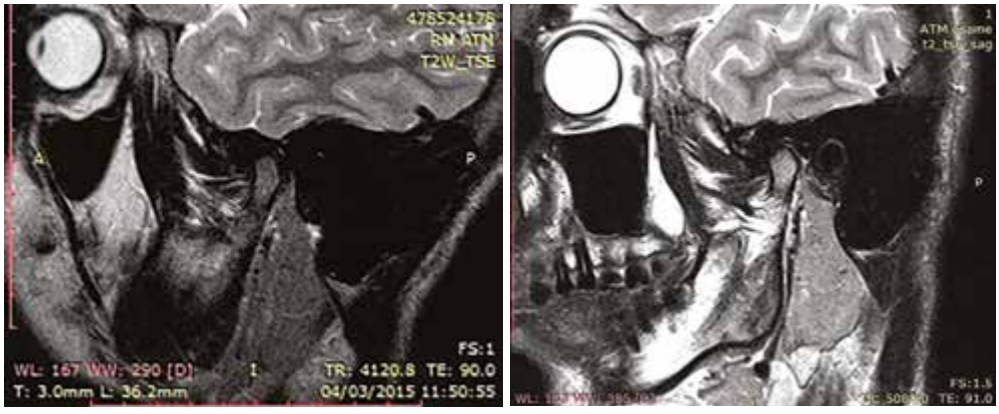

FIG. 3 Sagittal Section MRI left TMJ. March 2015 (left) and November 2020 (right).

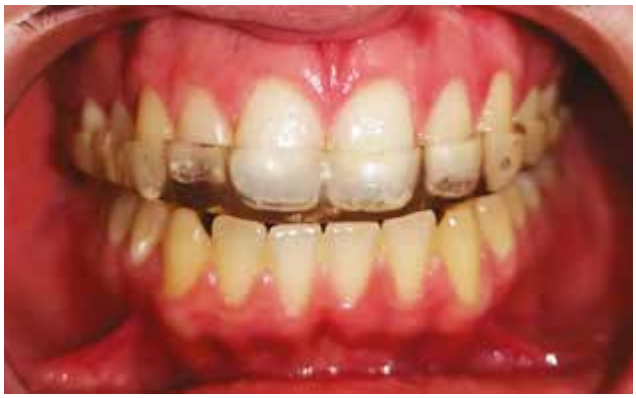

FIG. 4 Customised oral appliance.

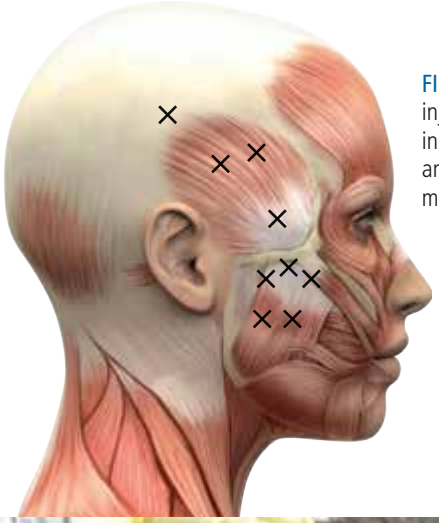

FIG. 5 BoNT-A injection points in masseter and temporalis muscles.

FIG. 6 BonT-A injection in the left temporalis muscle.

displacement of the disc with reduction on both sides. A slight resorption of the condylar head with small effusion in the retrodiscal area was also detected in the left TMJ (Fig. 2, 3). The patient was then diagnosed with persistent MP in the left masseter, bilateral disc displacement with reduction, and retrodiscitis and capsulitis in the left TMJ. Since there was no joint block, the limited mouth opening was due to a muscular contracture that has been structured for a long time. In addition to the previous recommendations, clonazepam was prescribed, 5 drops before bedtime, to control nocturnal bruxism and naproxen, 250 mg twice/day per 5 days, to manage joint pain and inflammation. At the follow-up visit in April, the patient reported only a slight improvement in jaw function and the VAS pain level was rated 7/10. It was therefore decided to fabricate an OA, a bite as described elsewhere [Viscuso,2020] (Fig. 4).

For the following 3 months symptoms further reduced, but in September pain raised again and muscle contracture and tenderness were still detected under palpation. BoNT-A infiltration was then performed in the masseter and temporalis area with a total of about 120 U of drug at the Pain Centre of the Businco Oncological Hospital in Cagliari: 40 U were injected in the masseter and 20 U in the temporalis muscle, on both sides. The patient was asked to clench teeth to properly identify the muscles to be injected and then multiple injections were performed covering on average a 2-cm skin surface over the target muscle tissue. Five injections were performed in the masseters and four in the temporalis muscles (Fig. 5, 6).

After one month, jaw range of motion significantly improved. Passive mouth opening was 41 mm and right and left lateral excursions were both 6 mm. The patient reported to feel more relaxed muscles and less tenderness, and the clinical exam confirmed the reduced tone of the masseter muscles. Reduced awake clenching of teeth was also referred, supposedly because of muscle weakness. Joint noises increased, probably due to the greater degree of mobility of the condyles. In November, mouth opening increased up to 45 mm, with no differences under forced assistance, and right and left lateral excursions up to 7 mm each. Pain completely disappeared. The patient was then recommended to continue to follow the above mentioned recommendations during the day and to wear the OA during sleep in order to control awake and sleep bruxism. Follow-up appointments were scheduled every 6 months for the following 6 years.

Currently, January 2022, the patient does not report any pain, tenderness under palpation or jaws' movements dysfunction. Mouth opening is 44 mm (Fig. 1), with no difference under forced assistance, and lateral excursions are 7 mm on each side. Quality of life completely recovered and the patient is attending the university with self-reported satisfactory results.

Discussion and conclusion

The present work discusses the management and the 7-year follow-up of a successfully treated adolescent male patient with bruxism and persistent MP by ,means of a single injection of BoNT-A. Investigations on the use of BoNT-A have expanded over the last two decades and currently its clinical use for certain types of pain is increasing. However, BoNT use in children and young adolescents with orofacial pain has not yet been investigated. It has both antinociceptive and anti-neurogenic inflammatory activity acting at both peripheral and central sites. BoNT-A has been demonstrated to inhibit the release of both Substance P and Calcitonin Gene-Related Peptide in ganglia [Welch, 2000; Durham, 2004], and of glutamate from primary afferent terminals [Cui, 2004]. Additionally, it has been demonstrated to block mechanical suprathreshold nociception supporting the idea of an inhibitory effect on nonselective cation Transient Receptor Potential channels (TRP) [Burstein, 2014]. In the light of the capability of BoNT to act both as a paralytic and antinociceptive agent, although separately, its clinical use could be justified in treating persistent MP and controlling bruxism when necessary.

We described the case of a young patient with a complex and long-lasting TMD, where both the muscular and the articular components were ipsilaterally affected and with a positive

history for sleep and awake bruxism. Since conservative first-line therapies failed in achieving satisfactory pain reduction and muscle relaxation, we were strongly motivated to perform BoNT-A injection. Recently, Guarda-Nardini et al. [2008] demonstrated that BoNT-A improved both objective (i.e. jaw movements) and subjective (i.e. pain) variables in patients with MP and sleep bruxism after a single injection. Similarly, Hosgor et al. [2020] showed significantly enhanced range of mandibular movements together with up to 70% reduction in pain among people with refractory MP and, again, sleep bruxism. Both studies, however, reported only six months of follow up. BoNT-A was demonstrated to reduce tenderness to palpation and pain compared to placebo [De la Torre Canales, 2020; Kurtoglu, 2008]. A recent systematic review and meta-analysis [Khalifeh, 2016] confirmed the long-term efficacy of BoNT-A compared to placebo, although no significant differences emerged over the first two months after injection. However, as BoNT-A appeared to be at least effective as OAs both in the short and long term, conservative treatment should be preferred still today [De la Torre Canales, 2020].

Concerning bruxism, the patient reported an improvement in reduced bruxism- related behaviours and muscle relaxation immediately after a single BoNT-A injection, at least about awake bruxism. The authors correlated the reduced bruxism-related behaviours to the masticatory muscles' weakness provoked by BoNT-A.

More recently, the ecological momentary assessment (EMA) approach has been optimized and made more objective using smartphone applications and should be recommended [Manfredini, 2020].

Data concerning the clinical use of BoNT for bruxism are limited to sleep bruxism; De la Torre Canales et al [De la Torre Canales, 2017] highlighted that BoNT represents a promising option for the management of SB consequences rather than for SB itself. BoNT, indeed, may reduce the intensity of RMMA contractions but not the number of episodes since RMMA episodes are under the influence of the brainstem arousal-reticular ascending system [Lavigne, 2006].

In conclusion, through the presentation of the current clinical case, the authors suggest that BoNT-A could be an optimum treatment for persistent MP and bruxism in young adolescents when first-line therapies fail. A single injection of BoNT-A supposedly stopped the vicious circle of bruxism-induced muscular pain and hypertone, at that point additionally aggravated by central processes, and, along with proper self-control and OA, restored the disorder without the need for further interventions.

Conflict of Interests

All authors disclose no financial and personal relationships with people or organizations that could inappropriately influence this manuscript.

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