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Treatment of Bruxism by Injection of Botulinum Toxin Into Trigger Points: Practical Guide and A New Technical Procedure for an Effective Result

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Abstract:

Objectives:

Bruxism is a debilitating condition that causes pain and damage in the stomatognathic system. Although botulinum toxin is recognized as effective in treating bruxism, it is still reserved for severe cases. To date, injection methods and procedures are not standardized, unlike cosmetic uses, leading to divergent results. This report aims to exhibit a novel technical injection and procedures that allow effective and efficient treatment of bruxism while highlighting its analgesic and anti-inflammatory effects.

Methods:

Toxin injections were applied to masseter muscle in trigger points to 67 patients, enrolled between 2009 and 2015, suffering from awake and sleep bruxism. All patients regardless of the duration of bruxism, their injection depended on the number of trigger points, performed in the same way in each session until full recovery. Descriptive statistics were performed to analyze the data using SPSS software.

Results:

Two groups of patients were individualized, G1 (bruxism duration of more than one year with previous use of occlusal splint) and G2 (recent bruxism without prior therapy). Patients in group G1 required more injection sessions and higher doses of toxin than patients in group G2 ($p<0.01$). The number of trigger points was also greater in group G1. As injection sessions progressed, the recovery time lengthened over time.

Conclusion:

This study validates our injection method and procedures using botulinum applied into trigger points and demonstrates its effectiveness at an early stage of bruxism at first-line therapy. The persistence of trigger points worsens bruxism, and injections must therefore be performed in these areas.

Keywords: Myofascial Pain Syndrome; Trigger Points; Botulinum toxin; Injection; Sleep Bruxism

Introduction

Bruxism, also considered a myofascial pain syndrome (MPS) of the stomatognathic system, causes tooth abrasion and mobility, fracture of implant, and failure of dental restoration with mild to severe orofacial pain affecting patient quality of life, social relation with overarching effects on society and costs on health care. Despite the availability of non-pharmacologic and pharmacologic treatment modalities, MPS remains challenging to treat with difficulty predicting results. BoNt-A injections are well recognized to be efficient in treating sleep and awake bruxism, However, there is no clinical protocol for using this toxin for orofacial pain.[1] Based on the twenty years of experience in this field using botulinum toxin type A (BoNt-A) with successful results highlighted by the enclosed retrospective study carried with significant statistical analysis ($p<0.01$), a practical guide for the therapeutic procedure and technique of injection using BoNt-A is provided in this work, that helps clinicians master this difficult disability.

To our knowledge, no study in the literature attributed the necessary doses of BoNt-A to the allocated number of trigger points. Additionally, this is the first study using BoNt-A injections applied to trigger points to treat bruxism with a long-term follow-up until full recovery.

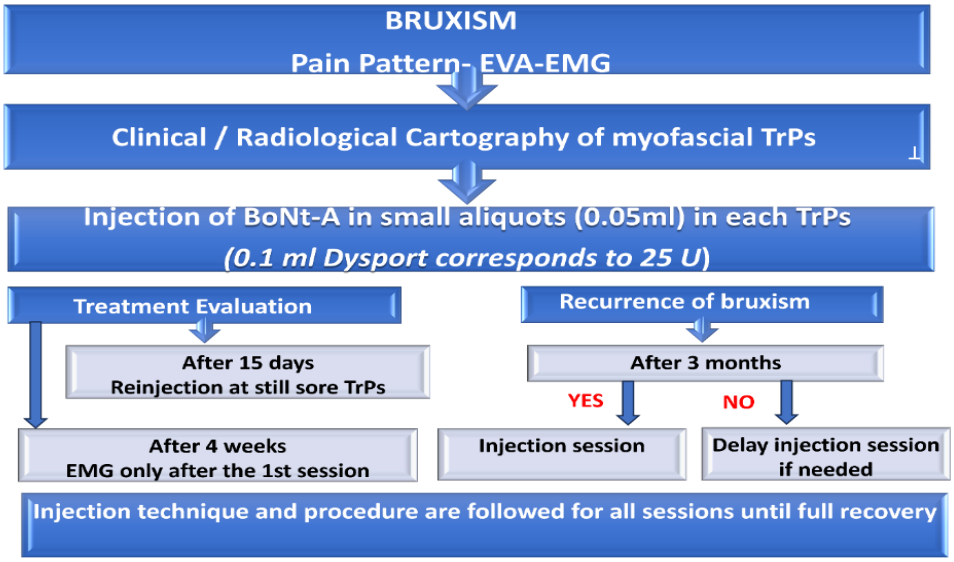
Methods:

The retrospective study enrolled 67 patients suffering from awake and sleep bruxism and fully recovered after BoNt-A injections during the period spanning between 2009 and 2015. The follow-up ranged from 16 to 55 months. This study has obtained ethics approval from the institutional committee review board and was conducted following the principles of the Helsinki Declaration and the rules of good clinical practice. Otherwise, this study is registered in clinicaltrials.gov.

The same therapeutic strategy was addressed for all bruxers using the same type of BoNt-A (Dysport, *Ipsen Pharma, Germany*), reconstituted with 0.9% sodium chloride solution so that 0.1 ml corresponded to 25 U. However, the recommended doses depended on the number of TrPs scattered, by careful palpation, in the masseter muscles where 0.05 ml was applied in each. Therefore, no standardized doses were defined but doses were tailored according to TrP's areas. Electromyographic (EMG) *testing* was used solely before the first session and 4 weeks later to assess the decrease in the force bite and to strengthen the patient's motivation in compliance with the therapeutic plan. According to the recovery time, repeated injections of BoNt-A were performed until full recovery (Figure 1).

The level of statistical significance, using SPSS software, was set to $p < 0,01$. The Chi-square test and ANOVA table were applied to compare data related to the technical procedure and results (injection sessions, doses of toxin, number of TrPs, recovery duration, and recurrency) between two groups according to the evolution of bruxism.

Figure 1: Practical guide of injection technique, with BoNt-A, and therapeutic procedure for bruxism



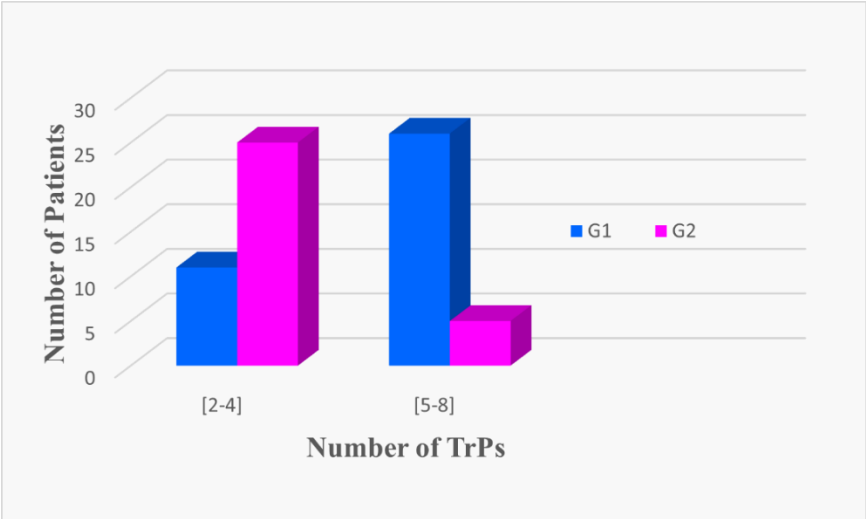
Results:

Two groups almost equal in number of patients were individualized:

- Group G1 (37 patients), with continued bruxism for more than one year and unsuccessful pain alleviation with a prior occlusal splint.
- Group G2 (30 patients), with bruxism for less than one year without previous therapy.

All the individuals, with significant female representation in both groups, experienced pain relief from the 4th to 10th days after the injection session with a varying recovery duration for each patient. Moreover, recurrences occur faster and more frequently in group G1. Besides, the greatest number of TrPs was mainly detected in group G1 where 69% of them had more than 5 TrPs, unlike in group G2, a similar number of TrPs was found in only 16% of patients (Figure 2). Consequently, patients belonging to group G1 needed higher doses of toxin than those of group G2 as revealed in the statistical analysis ($p<0.01$). It was found that the average total doses required for full recovery were 420 U and 180 U for groups G1 and G2, respectively.

Figure 2: Distribution of TrPs in both groups G1 and G2. A higher number in patients of group G1



Pain alleviation assessed with the Visual Analogue Scale was objectively correlated with EMG results showing a decrease in the peak amplitude of EMG bursts, and consequently in the intensity of masseter contraction one month after toxin injection. However, pain relief lasted differently and recurrences were greater in group G1 requiring more injection sessions (Table 1).

Table 1: Recovery duration according to injection sessions in both groups

	1st session	2nd session	3rd session
G1 Recovery duration (*Months*)	**4-6**	**6-9**	**12-18**
G2 Recovery duration (*Months*)	**6-9**	**12-18**	**Full Recovery**

First of all, 21,6% of group G1 had 4 injection sessions while none of the patients of group G2 required a 4th session. On the contrary, 20% of group G2 observed complete healing with only one session while none of the patients in group G1 had the same fate. Additionally, more than half of the patients of group G1 required Three session injections mostly with high doses of BoNt-A. On the other hand, an equal proportion of group G2 required low doses usually performed in only two sessions, and achieving full recovery. Generally, the more the bruxism was continued as in group G1, the more TrPs were developed and injection sessions were more required (Figure 3).

Repeated measure ANOVA revealed that $p < 0.01$ concluded a statistically significant difference between the two groups regarding the number of injection sessions, doses of BoNt-A, number of TrPs, and recovery duration (Table 2).

Figure 3: Distribution of patients according to injection sessions and TrPs numbers

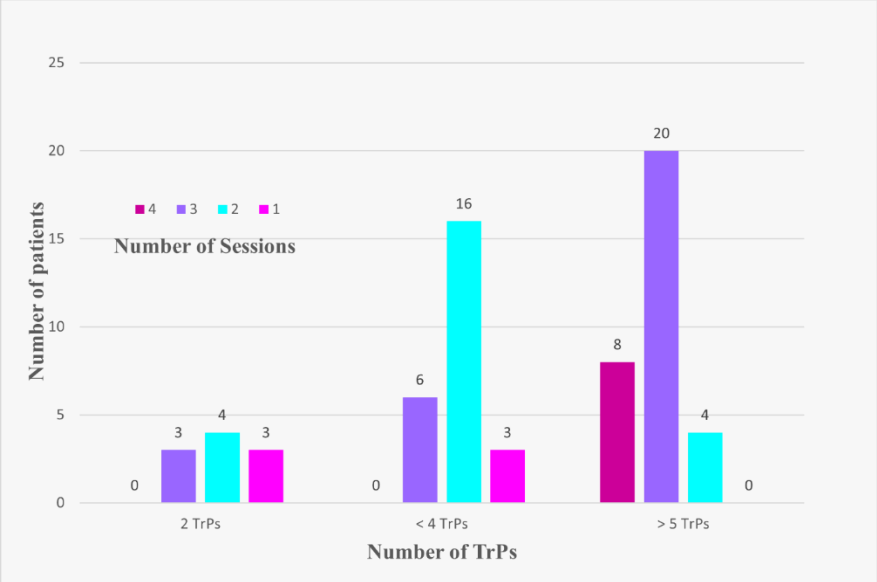


Table 2: ANOVA table

			Sum of squares	Degrees of freedom	Mean squares	F	p
injection sessions * G1/G2	Inter groups	(Combined)	19,589	1	19,589	51,222	<,001
	Intra-groups		24,859	65	,382		
	Total		44,448	66			
Total doses * G1/G2	Inter groups	(Combined)	999936,668	1	999936,668	39,187	<,001
	Intra-groups		1658608,108	65	25517,048		
	Total		2658544,776	66			
TrPs * G1/G2	Inter groups	(Combined)	60,547	1	60,547	23,127	<,001
	Intra-groups		170,169	65	2,618		
	Total		230,716	66			
After 1st session * G1/G2	Inter groups	(Combined)	213,852	1	213,852	379,212	<,001
	Intra-groups		36,656	65	,564		
	Total		250,507	66			
After 2ned session * G1/G2	Inter groups	(Combined)	1475,402	1	1475,402	830,572	<,001
	Intra-groups		115,464	65	1,776		
	Total		1590,866	66			

Discussion:

Although the increasing use of botulinum toxin is primarily for cosmetic treatment, there is a lack of accuracy and a standardized technical procedure for the treatment of bruxism, leading to non-contributory results that are often reported with follow-up at short-term. Thus, controversies and unequivocal opinions generate an easy abandonment of this therapy or reserve it for severe bruxers who are refractory to conventional methods.[2,3]

Meta-analysis and systematic reviews of randomized control trials about the treatment of bruxism usually lead to practically identical and redundant conclusions such as: "*noncontributing study, short-term follow-up, non-standardized methodology, incomparable results*" or "*toxin reserved for severe cases of bruxism*".[4,5] However, we claim the latest opinion which is against our contributive results showing that the use of BoNt-A at the onset of bruxism is more efficient and leads to full recovery using fewer doses of toxin because TrPs are still rare. So, fewer injection sessions due to greater recovery time allow less laborious treatment of bruxism with lower financial costs (Supplementary Table 2). Although the protective aspect against teeth wear of an occlusal splint is commonly admitted in conventional treatment, it does not solve the cause of bruxism explaining its failure in mastering bruxism.[6] Furthermore, recent systematic reviews did not find evidence to support splint use for temporomandibular disorders or bruxism which is also demonstrated in all individuals of group G1 who showed no improvement in their bruxism despite using occlusal splints for up to four years before performing toxin injections.[7,8]

The hallmark of MPS is admitted to be related to the muscle itself. It stems from TrPs which are tight knots between muscle and fascia. They are foci of chronic pain with a refereed pattern due to the neuropathic component. So, although the complex mechanism of this worldwide disability is still poorly understood, it is important to take a broad view as we endeavor to understand the complex bio-physiology of myofascial pain related to bruxism and the therapeutic implications for efficient results. Therefore, treatment centered on TrPs, which are pain stems, and decreasing the bite force by decreasing the force contraction of the masticatory muscle is a meaningful and relevant treatment strategy. TrPs are found as palpable « rope-like » nodularity that causes pain and reproduces the patient's referred pain pattern when pressure is applied. Their detection is mandatory to perform BoNt-A injections. TrPs are scattered randomly and can be active or quiescent known as latent trigger points which are subclinical neuromuscular lesions that reveal pain when compressed but do not spark spontaneous complaints. However, they can be converted on active TrPs when continuous detrimental stimuli are applied notably sustained muscular contraction causing ischemia.[9] On the other hand, unskilled palpation can hamper detecting these points and downregulate the required doses of BoNt-A leading to insufficient results. So, ultrasound diagnosis of TrPs appears to help clinicians, showing discrete, focal, hypoechoic regions with an elliptical shape that looks like a speckling area.[10] In addition, due to local ischemia and injury stimuli, the release of neuropeptide and inflammatory mediators such as bradykinin, substance P, Glutamate, and potassium trigger peripheral nociceptive nerve endings causing peripheral sensitization. This process is reversible so that TrP activity and pain intensity are proportional to the mechanical stress of the muscle.[11] Thus, it is obvious that pain gets exacerbated when muscle cramping appears, as observed in bruxism especially when it lasts for an extended period, so that prolonged ischemia causes muscular damage and multiplication of active TrPs number. This is confirmed by this study showing that patients in group G1 had a significantly higher number of TrPs than patients in group G2. Thus, the more significant the number of TrPs, the greater the pain and the higher the required doses of BoNt-A. This study concludes that the

persistence of continued bruxism causes its progressive aggravation with longer, more laborious, and expensive treatment. Furthermore, the study's results highlighted that early therapy offered a longer recovery duration, fewer required doses of toxin, and full recovery was reached with fewer injection sessions. At first glance, the financial impact will undoubtedly be positive regarding the treatment cost and individual productivity.

The well-known pharmacologic action of BoNt-A is naturally the inhibition of acetylcholine-mediated neuromuscular transmission at the motor end plate causing muscular paralysis.[12] Otherwise, it has been shown that spontaneous electric activity was identified in the TrP site and non-identified in non TrP site which highlights the importance of the injection-based therapy centered on TrPs with small aliquots of solution resulting in muscular relaxation around the area of the TrP.[13] On the other hand, wakefulness and care concerning the injected volume are crucial because injecting a large volume into a small muscle can give rise to ischemia, muscle necrosis, later fibrosis, and muscle contracture which unbalance the effect of the toxin and create iatrogenic side effects.[10]

The reduction of pain with BoNt-A injection was originally assumed to be due to muscle relaxation and the decrease of the mechanical stress of the masseter muscle, which is the target location of TrPs in the human body.[14,15] In addition, there is growing evidence that nociceptive neurotransmitters (Substance P, Glutamate, and Calcitonin-gene-related-peptide CGRP) and other biomarkers (NR2B, Nerve growth factor) play a crucial role in nociceptive processing in the peripheral nerve ending in the masseter muscle and orofacial pain.[16] On the other hand, numerous studies have shown that BoNt-A directly decreases the release of CGRP from trigeminal neurons, blocks the release of nociceptive neurotransmitters from afferent nerve endings, and reduces TRPV1 expression in the nociceptors leading to peripheral desensitization and results in attenuation of inflammation and offering pain alleviation. Moreover, BoNt-A inhibits further central sensitization by retrograde axonal transport pathways to the central nervous system.[17,18] This reduction in pain typically occurs a few days after BoNt-A injection preceding muscle relaxation.[19] In summary, BoNt-A injections decrease pain and act against tooth wear in bruxism by normalizing muscular hyperactivity and halting ischemia which causes muscle damage multiplying TrPs. Besides, inhibitory effects on nociceptors of peripheral and central nervous systems are relevant and need further exploration.

In conclusion, As TrPs may play a major role in the genesis of bruxism, and constitute the starting point of pain, which is aggravated by sustained muscular contraction causing ischemia that promotes the release of nociceptive neurotransmitters, it is clear that BoNt-A injection in these areas has a mechanical and pharmacological effect on both pain and bite force intensity. Based on this study's results highlighting the correlation between TrPs, pain intensity, and bruxism duration, it appears that the use of BoNt-A injections should be proposed as the first-line treatment for bruxism, particularly when taking into account the nociceptive effect and the neuronal modulation of this toxin. We emphasize the efficacy of BoNt-A injection applied in TrPs with modulated doses based on their number with regular follow-up to repeat injection sessions when bruxism recurs until full recovery as explained in the practical guide for injection technique and therapeutic method. This allows clinicians to master this disability leading to effective results that are easier to obtain when bruxism is recent.

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