The Effect of Different Doses of Botulinum Toxin on Masseter Muscle in Patients with Bruxism

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Background and Objectives: Botulinum toxin type A is produced by clostridium botulinum. It acts by inhibiting the release of acetylcholine from cholinergic neurons. Botulinum toxin has been used for management of bruxism, which is a parafunctional disorder and characterized by clenching or grinding of the teeth or both. This study aimed to find out the effect of two different doses of injecting botulinum neurotoxin in masseter muscle in a patient with bruxism.

Materials and Methods: A prospective clinical open trial study was conducted from November 2018 to November 2019. Thirty patients, aged 20-45 years, with bruxism were subjected to injection of two different doses of botulinum toxin in masseter muscle. Patients were divided into two equal groups. The first group included 15 patients treated by 18 units of botulinum toxin, 9 units for each side and the second group included 15 patients treated by 24 units of botulinum toxin 12 unit for each side. Parameters, as visual analogue scale (VAS), Bite force, patient's evaluation of lower facial slimming were recorded for each patient before and after the injections of botulinum neurotoxin at 2 weeks, 4 weeks and 3 months.

Results: The study showed a significant reduction in VAS, bite force and patient's evaluation of facial slimming for both groups after 2 weeks, 4 weeks and 3 months of follow up (P *< 0.05) with no significant differences in both group doses.*

Conclusion: Both doses of botulinum toxin (18 and 24) units have significantly improved pain score, and bite force and have the same efficacy in treating patients with bruxism., therefore dose of 18 units of the drug is preferable over 24 units in treating bruxism.

Keywords: Bruxism, Botulinum Toxin, Masseter muscle, VAS, Bite force.

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Introduction

Bruxism is a parafunctional disorder characterized by clenching or grinding of the teeth or both, which affects about 20% of the population. It is caused by the activation of reflex chewing activity.[1] Marie Pietkiewicz introduced the term 'la bruxomanie' for the first time in 1907, and it was later changed to 'bruxism'.[2] Bruxism is of great interest to dentists, as well as psychologists, neurologists, and other medical professionals. It has many causes, including occlusal disorders and stress. However, the exact cause is still unknown.[3] Bruxism can affect people during the day or at night during sleep. Wakefulness bruxism or daytime bruxism can be defined as 'clenching' and is semi-voluntary, it has many names, including awake bruxism and diurnal bruxism. Daytime bruxism can be triggered by stress or studying for exams. Sleep bruxism can be defined as teeth grinding or clenching.[4] Bruxism occurs most in younger populations.[5]

Bruxism can be diagnosed by certain intraoral and extraoral clinical signs, such as attrition, tooth fracture, tooth pain, headache or masseter or temporalis muscle hypertrophy.[6]

The aetiology of bruxism is complex. The most common factor is the psycho-emotional and mental health of bruxers. Lo-cal, systemic and neurological factors must also be considered. Local factors include occlusal problems, bad restorations and malocclusions.[7] certain medications, upper respiratory tract problems and smoking are risk factors for bruxism.[8]

The symptoms of bruxism can be treated with pharmacotherapy, physiotherapy or oral appliances such as occlusal splints.[6] Pharmacotherapy options useful for managing bruxism include botulinum toxin type A and antidepressants. However, anti-depressants, such as amitriptyline, have certain side effects, such as daytime drowsiness and dry mouth.[9] currently, the most advanced pharmacological approach for managing bruxism symptoms is to inject botulinum toxin into the masticatory muscles. This is very effective for controlling involuntary orofacial movements.[10]

This study aimed to find out the effect of two different doses of injecting botulinum neurotoxin in masseter muscle in a patient with bruxism.

Methods

The study is a prospective clinical open trial, involving 30 volunteers of both genders, aged 20–45 years. The study was conducted in the city of Erbil (Outpatient clinic-collage of Dentistry at Hawler Medical University) and Koya (Koya Dental Center). The study period began in November 2018 and ended in August 2019.

Inclusion criteria: Moderate to severe pain of the masseter muscle and the temporomandibular joint area related to bruxism during clinical examination, patients aged 20–45 years with tooth grinding sounds corroborated by family mem-bers or caregivers, also cases where bruxism resulted in occlusal surface at-trition of posterior teeth, present of masseter muscle hypertrophy upon voluntary forceful clenching, Tongue and cheek indentation, and Presence of masseter muscle hypertrophy on voluntary contraction.

Exclusion Criteria: Pain in the oro-facial region, known allergy to botulinum toxin, neuromuscular disease or bleeding disorders, Antibiotic therapy and pulmonary disease that produces coughing du-ring sleep or infectious skin lesions at the site of the injection.

The study involved 30 patients with bruxism, who were divided into two groups of 15 patients. According to the pilot study doses of 18 and 24 units have been selected for this study. The first group of patients received 18 units (10 units equal to 0.5 ng of clostridial protein) of botulinum neurotoxin. Each patient received 9 units injected at three points on each side of the masseter muscle. The second group received 24 units of botulinum neurotoxin, 12 units injected at three points each side of the masseter muscle. The following parameters were recorded for each patient before the injections of botulinum neurotoxin and after the injections at 2 weeks, 4 weeks and 3 months.

The study protocol was approved by the institutional ethical committee of the College of Dentistry at Hawler Medical University, and a written consent form in the patients' mother language was signed by all patients before the study was conducted.

The parameters

1. Pain scores

This parameter was measured using a visual analogue scale. For the evaluation of post-operative pain, visual analogue scale forms were completed by the patients, who rated the degree of pain on a scale of 0 (absence of pain) to 10 (maximum pain) before the injections and 2 weeks, 4 weeks, and 3 months after the injections.[11]

2. Bite force

We used a dental bite force device which included a testing load cell to record bite force. The patients were seated in an upright position and were trained beforehand to perform the strongest bite over the device for 3–4 seconds.[12] The bite force measurements were taken from the first molar region.[13]

3. Patients' evaluations of lower facial slimming. There were five possible choices for patients' evaluations of improvement after treatment: 0 (no improvement or worsening of the condition), 1–24% (discrete improvement), 25–49% (mild improvement), 50–74% (moderate improvement) and 75–100% (considerable improvement).[14]

Procedures. Botulinum Toxin type A is a lyophilized powder that requires reconstitution with sterile saline. Therefore, Botulinum Toxin diluted in 2 cc of 0.9% sodium chloride solution.[15]

Botulinum toxin injections for masseter muscle are commonly performed procedures that achieve good results and safety profiles. Appropriate dosing, injection location, and injection depth were key factors for achieving the desired result with minimal complications. Before injection, the safe site injection of botulinum toxin in masseter muscle was performed by using Peng and Peng's method.[16] keeping injections inside the safe zone, and ideally in 3 different locations at least 1cm from any border, is crucial to prevent common side effects (Figure 1). Aspiration was performed before the botulinum Toxin was injected to avoid possible intravascular deposition.[17]

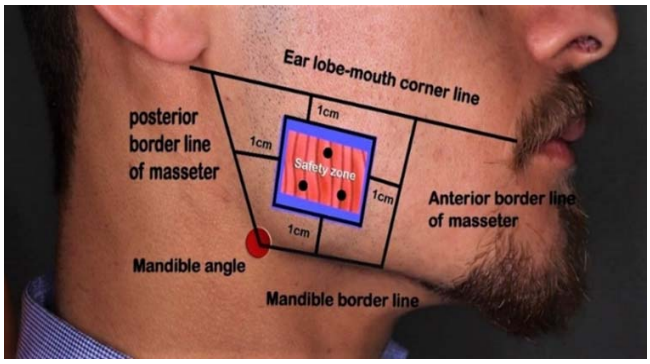

Figure 1: The ideal injection safe zone of 1cm away from each border of one of the patients in this study.

Results

The demographics and baseline characteristics shows that the mean age for the first group was (27.8 ± 5.1) and the mean age for the second group was (28.06 ± 5.7), gender and marital status as a demographic part and it is not significant for both groups, on the other hand, the parameters; visual analogue scale and bite force (kg) for both groups (18 and 24) units were not significant from baseline as shown in Table 1.

Table 1: The demographics and baseline characteristics of both groups.

Variables	18 unit		24 unit		P-value
Mean Age	27.8 ± 5.1		28.06 ± 5.7		0.89
Gender	Male	female	Male	Female	0.64
	6 (40%)	9 (60%)	9 (60%)	6 (40%)	
Marital status	Single	Married	single	Married	0.71
	10 (66.7%)	5 (33.3%)	8 (53%)	7 (46.7%)	
VAS	6.93 ± 2.4		6.5 ± 2.26		0.64
Mean bite force right side (kg)	60.86 ± 18.15		71.56 ± 29.33		0.16
Mean bite force left side (kg)	62.8 ± 16.87		73.38 ± 22.79		0.24

The Effect of Botulinum Toxin Measured by a Visual Analogue Scale. The patient's pain score was decreased after 2 weeks of injections of 18 units of botulinum toxin (9 units per side), these changes statistically were significant (P-value of <0.0001). However, the pain scores did not change significantly between the 2-week, 4-week, and 3-month follow-ups as shown in Table 2.

The results in Table 3 shows that the patients' pain score decreased after 2 weeks of injections of 24 units of botulinum toxin (12 units per side) these changes statistically were significant (P-value of <0.0001). However, the pain score did not change significantly between the 2-week, 4-week, and 3-month follow-ups.

Table 2: The effects of injections of 18 units of botulinum toxin to the masseter muscle according to the results of a VAS for measuring pain before injections and 2 weeks, 4 weeks and 3 months.

Times	No pain	Mild	Moderate	Severe	P-value
Before	0 (0%)	3 (20%)	2 (13.3%)	10 (66.7%)	
After 2 weeks	13 (86.7 %)	0 (0%)	2 (13.3%)	0 (0%)	<0.0001
After 4 weeks	14 (93.3%)	0 (0%)	1 (6.7%)	0 (0%)	
After 3 months	14 (93.3%)	0 (0%)	1 (6.7%)	0 (0%)	

Table 3: The effect of injections of 24 units of botulinum toxin to the masseter muscle according to the results of a VAS for measuring pain before injections and after 2 weeks, 4 weeks and 3 months.

Times	No pain	Mild	Moderate	Severe	P-value
Before	0 (0%)	2 (13.3%)	5 (33.3%)	8 (53.3%)	
After 2 weeks	11 (73.3 %)	4 (26.7%)	0 (0%)	0 (0%)	<0.0001
After 4 weeks	9 (60%)	5 (33.3%)	1 (6.7%)	0 (0%)	
After 3 months	10 (66.7%)	4 (26.7%)	1 (6.7%)	0 (0%)	

Patients' Evaluations Regarding Lower Facial Improvement after Administration of Botulinum Toxin. According to Table 4, 2 weeks after the injections, there was no improvement in patients' evaluations, but after 4 weeks, the evaluations started to improve. Seven patients reported discrete improvement and eight patients reported no improvement. After 3 months, six patients reported discrete improvement (40%) and three patients reported mild improvement (20%). These results indicate a statistically significant improvement after injections of 18 units of botulinum toxin.

The results in Table 5 indicating improvements in patients' evaluations of lower facial slimming after injecting 24 units of botulinum toxin (12 units per side) shows that two patients reported discrete improvement after 2 weeks (13%). After 4 weeks, six patients reported discrete improvement (40%) and two patients reported mild improvement. After 3 months patient's improvements increased to six patients reporting discrete improvement (40%), five patients reporting mild improvement (33.3%) and two patients reporting moderate improvement (13.3%).

Table 4. Patient's evaluations regarding lower facial improvement 2 weeks, 4 weeks, and 3 months after injections of 18 units of botulinum toxin (9 units per side).

Times	None	Discrete	Mild	Moderate	P-value
After 2 weeks	15 (100%)	0 (0%)	0 (0%)	0 (0%)	
After 4 weeks	8 (53.3%)	7 (46.7%)	0 (0%)	0 (0%)	0.0017
After 3 months	6 (40%)	6 (40%)	3 (20%)	0 (0%)	

Table 5. Patients' evaluations of lower facial slimming after 2 weeks, 4 weeks, and 3 months of injections of 24 units of botulinum toxin (12 units per side).

Times	None	Discrete	Mild	Moderate	P-value
After 2 weeks	13 (86.7%)	2 (13.3%)	0 (0%)	0 (0%)	
After 4 weeks	7 (46.7%)	6 (40%)	2 (13.3%)	0 (0%)	0.0018
After 3 months	2 (13.3%)	6 (40%)	5 (33.3%)	2 (13.3%)	

Comparison of the Mean Differences for Pain and Bite Force Before and After Injections of Botulinum Toxin. Tables 6, 7 shows comparing the mean before and after injections for 18 units and 24 units of botulinum toxin, respectively, show significant changes in vas parameter and bite force between before and after injections but no significant change between 2 weeks, 4 weeks and 3 months after treatment.

The results in Table 8 showing the mean percentage change 3 months after administration of the treatment indicates that there was no significant difference between the two groups.

Table 6. Comparison of mean and standard deviation for pain and bite force before and 2 weeks, 4 weeks and 3months after injections of 18 units of botulinum toxin.

	Before	After 2 weeks	After 4 weeks	After 3 months
VAS	6.93 ± 2.4 A	0.93 ± 1.33 B	0.73 ± 1.27 B	0.86 ± 0.99 B
Bite force, right side (kg)	62.8 ± 16.8 A	45.9 ± 11.53 B	45.6 ± 11.45 B	46.2 ± 12.5 B
Bite force, left side (kg)	60.8 ± 18.1 A	42.7 ± 11.6 B	41.9 ± 13.5 B	43.4 ± 12.9 B

Different letters indicate significance at P <0.05

Table 7. Comparison of mean and standard deviation for pain and bite force before and 2 weeks, 4 weeks and 3 months after injections of 24 units of botulinum toxin.

	Before	After 2 weeks	After 4 weeks	After 3 months
VAS	6.5 ± 2.26 A	0.66 ± 0.89 B	1.06 ± 1.33 B	1.13 ± 1.35 B
Bite force, right side (kg)	73.3 ± 22.7 A	47.7 ± 17.5 B	46.6 ± 15.06 B	47 ± 16.8 B
Bite force, left side (kg)	71.56 ± 29.3 A	46.6 ± 19.07 B	48.22 ± 17.93 B	48 ± 17.79 B

Different letters indicate significance at P <0.05

Table 8. Mean percentage changes in bite force and Vas before and after 3 months of injections of 18 units and 24 units of botulinum toxin.

	18 unit	24 unit	P-value
Bite force, right side (kg)	25.5 ±12.94	35.22 ±12.70	0.803
Bite force, left side (kg)	26.82 ±14.7	31.81 ±10.78	0.130
VAS	88.8%	84.38%	0.96

Discussion

Bruxism is a very complex multifactorial disorder, the causes of which may be related to neurological or psychiatric disorders. Treatment of this disorder includes pharmacological approaches, such as botulinum toxin type A, and non-pharmacological approaches, such as mandibular advancement devices. In this study, botulinum toxin type A has been used as, only the A and B serotypes have been approved by the FDA for clinical use to treat bruxism and other conditions such as ble-pharospasm, cervical dystonia and forehead wrinkles.[18]

Past studies have reported that botulinum toxin type A provides longer and better pain relief than botulinum toxin type B.[19]

This study shows that the use of two different doses, 18 units (9 units to each masseter muscle) and 24 units (12 units to each masseter muscle), of botulinum toxin to the masseter muscle was effective for the management of bruxism symptoms. The study was conducted using a VAS to measure pain, as a first parameter, in patients with bruxism. There was a significant reduction in the pain score for both group after administration. However, the values after 2 weeks, 4 weeks and 3 months were similar to each, which shows that there were no significant improvements between these follow-ups.

The outcomes of our study are similar to the results reported by Asutay et al. (2017).[20] who used 20 units to each of the masseter muscle, They observed that after 6 months pain VAS score had started to increase gradually.

The second parameter which was bite force (kg) was measured between the upper and lower first molars on both sides using a dental bite force testing load cell. Local injection of botulinum Toxin after three months caused a significant reduction in bite force in both groups. This improvement in

bite force induced by botulinum is due to a relaxation of the skeletal muscles through blocking the calcium-mediated release of acetylcholine from motor nerve endings.[21]

The bite force values for all postoperative time points were similar. The results of this study is in agreement with song *et al.* (2014) in which T-Scan system was used for measuring occlusal force during maximum biting and followed by a reduction of bite force.[22]

On the other hand, Lee *et al.* (2010) used electromyography for his study. They found that the number of suprathreshold were decreased at 4 weeks after administration of botulinum toxin to the masseter muscle.[23]

The third parameter was improvement with regard to lower facial slimming according to patient's evaluations. Most patients with bruxism have masseter hypertrophy due to hyperactivity of this muscle. After three post-injection follow-ups, the first group reported minimal to mild improvement, but the second group reported better results (13.3%) with those patients noticing moderate improvement after 3 months. However, the differences between the two groups were not significant. The outcomes of this study are similar to those of study reported by Klein *et al.* (2014).[14] who showed that injection of high doses of botulinum Toxin (90 units) improved lower facial slimming and decreased masseter hypertrophy.

Conclusion

Both doses of botulinum toxin (18 and 24) units have significantly improved pain score, and bite force and have the same efficacy in treating patients with bruxism., therefore dose of 18 units of the drug is preferable over 24 units in treating bruxism.

Conflicts of interest

The authors reported no conflict of interest.

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