BOTULINUM TOXIN TYPE-A…AN EVOLVING TREATMENT MODALITY IN THE MANAGEMENT OF TEMPOROMANDIBULAR JOINT DISC DISPLACEMENT

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ABSTRACT

INTRODUCTION: Temporomandibular disorders (TMD) is an umbrella term embracing a set of conditions that affect the masticatory muscles and the temporomandibular joint (TMJ) .Internal derangements, specifically disc displacement with reduction (DDr), are one of the major findings in TMD . For the treatment of DDr, occlusal appliances and some pharmacological agents were suggested. Several studies were done evaluating the therapeutic use of Botulinum Toxin Type A (BTX-A) in TMD of myogenic origin. But only few studies investigated its effect in the management of TMD of arthrogenic origin.

OBJECTIVES: This study was done to evaluate the effect of Botulinum Toxin Type A (BTX-A) injection in the lateral pterygoid muscle (LPM) with and without anterior repositioning appliance (ARA) as a treatment modality for DDr.

MATERIALS AND METHODS: Eighteen patients with anterior disc displacement with reduction (DDr) as diagnosed clinically using Research Diagnostic Criteria (RDC/TMD) and confirmed by MRI were enrolled in this study. Patients were randomly assigned into three groups each comprising 6 patients. Group I received ARA, group II received BTX-A while group III received both treatment modalities. After 3 months, evaluation was done subjectively through Helkimo Anamnestic index (Ai) and objectively through electromyography (EMG) as well as MRI.

RESULTS: Clinically, there was significant improvement in TMD symptoms in the three studied groups, while disc position was significantly improved in groups II and III as proved by MRI.

CONCLUSIONS: Anterior repositioning appliance is effective in treating patients with disc displacement with reduction; however, BTX-A with and without ARA proved to be a more valuable treatment modality in the management of disc displacement with reduction.

KEYWORDS: Botulinum Toxin, disc displacement, lateral pterygoid, electromyography

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INTRODUCTION

Temporomandibular disorder (TMD) is a term that refers to conditions affecting both TMJ as well as muscles of mastication. It includes myofascial pain, internal derangements in addition to other joint disorders as osteoarthritis and arthralgia (1, 2). According to the classification of RDC/ TMD there are three main types of internal TMJ derangement: disc displacement with reduction and disc displacement without reduction with or without limited mouth opening. The most common type is disc displacement with reduction (DDr) characterized by clicking in the TMJ (2-6).

Many etiologic factors have been reported causing DDr (7-9). One of these predisposing factors leading to DDr is the LPM activity (9). Since its close relation to the articular disc, poor coordination in the lateral pterygoid muscle (LPM) fibers is believed to be a possible cause for DDr (9-13). In 2016, kamble and Mitra (14) investigated the relation between the LPM and DDr and concluded that LPM attachment is related to DDr. Hiraba et al (15) studied the EMG activities of the two heads of the LPM in relation to mandibular condyle movement. He stated that a coordinated movement between the condyle and the articular disc is essential for smooth mandibular movements where the LPM muscle plays a crucial role in this coordination. He concluded that the position of the articular disc in relation to the maxilla is controlled indirectly by the inferior head of the LPM.

For the management of DDr, conservative treatment modalities as the use of physical therapy, pharmacologic therapy and occlusal appliances or combination of these treatment modalities should be considered prior to any surgical intervention (16-18).

Several designs of occlusal appliances including stabilization, anterior repositioning (ARA) and pivot appliances are effective in the management of DDr. However, ARA is believed to be the appliance of choice to be used in treating patients with DDr (19, 20). Furthermore, many pharmacological agents as analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), local anesthetics, corticosteroids, muscle relaxants and Botulinum Toxin injections proved to be effective in the management of TMD (16-18, 21, 22).

Botulinum Toxin (BTX) is an exotoxin produced from Clostridium botulinum. BTX inhibits the release of Acetylcholine at the presynaptic junction, producing a transient and dose- dependent reduction of muscle activity as well as the glands innervated, without creating systemic effects (21, 23). BTX is considered the “poison that heals”. There are seven serotypes of BTX that are given alphabetical letters from A to G. These serotypes vary in their biochemical and pharmacological actions with different exotoxin protein complex compositions (24, 25). Regarding its therapeutic effects, Botulinum Toxin Type A (BTX- A) is considered the safest and the most effective serotype with the longest duration of action (25, 26). Several studies were done evaluating the therapeutic use of BTX-A in TMD of myogenic origin (23, 27, 28). But only few studies investigated its effect in the management of TMD of arthrogenic origin as DDr (13, 29).

Therefore, the purpose of our study was to evaluate the effect of BTX-A injection in the LPM as an evolving treatment modality with and without ARA in the management of patients with DDr based on the assumption that the activity of the LPM plays a key role in the etiology of DDr.

MATERIALS AND METHODS

Ethical Considerations:

The clinical trial was explained to the patients and then informed consents were obtained from all the patients enrolled in our study. The study was performed after obtaining the approval of the research ethics committee, Faculty of Dentistry, Alexandria University.

Patient selection

Eighteen patients with TMJ clicking were selected from those attending the temporomandibular dysfunction clinic at the Prosthodontics Department, Faculty of Dentistry, Alexandria University.

Patients were selected according to strictly identified inclusion and exclusion criteria. The inclusion criteria were TMJ with audible and palpable click indicating DDr as also proved by MRI, in addition to the presence of full or nearly full complement of natural teeth. While the exclusion criteria were the presence of any degenerative diseases of TMJ, patients with DD without reduction, pregnant and lactating females, patients with known allergy to BTX-A, patients contradicted to undergo MRI or patients suffering from any neurological disorders.

Therapeutic Intervention

Before any treatment was done, all patients were examined clinically according to the research diagnostic criteria of TMD (RDC/TMD) (5). Patients that were included in this study were those diagnosed as RDC/TMD Axis I group II.a indicating DDr (5) and confirmed by MRI (Figures 1).

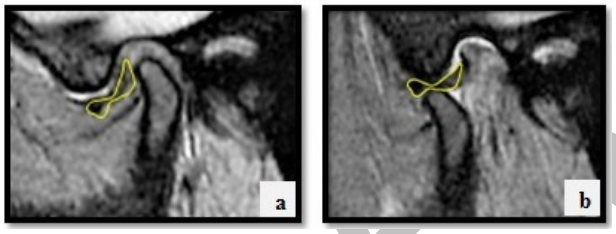

Figure 1: Oblique sagittal PD MRI sequence showing: a) anterior disc displacement in closed mouth position and b) in open mouth position where the articular disc is reduced confirming DDr. (articular disc outlined in yellow).

Then the patients were randomly assigned into three groups each including six patients.

Group I (n=6): Patients received maxillary anterior repositioning appliance (ARA).

Group II (n=6): Patients were given Botulinum Toxin Type A injection in the LPM under EMG-guidance.

Group III (n=6): Patients received maxillary ARA in addition to BTX-A injection in the LPM under EMG-guidance.

Maxillary ARA was fabricated according to Okeson (30) method. The patients were instructed to wear the appliance only at night for three months.

An EMG-guided (Dantec Clavis; Natus, USA) injection of 30 units of BTX-A (Botox; Allergan, CA) was done using intraoral approach to the LPM, without aiming to differentiate between both heads. The patient was asked to move the mandible contra-laterally to activate the LPM and ensure intramuscular injection (13, 29). (Figures 2, 3)

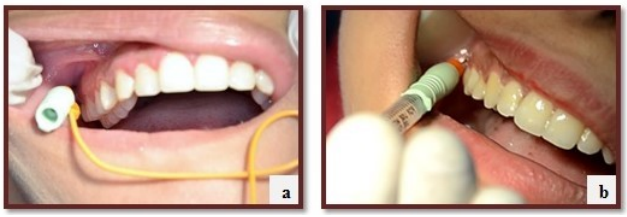

Figure 2: Showing a) The needle inserted in injected site lateral to the maxillary tuberosity and just above the maxillary molars. b) Injection of reconstituted BTX-A solution in the LPM.

Figure 3: Showing EMG-guided BTX-A Injection Procedure.

Subjective Clinical Evaluation

Clinical assessment of the severity of TMD symptoms was done before any treatment then after three months after the therapeutic intervention. The assessment was done using Helkimo Anamnestic Index (Ai) (31).

Objective MRI Evaluation

MRI was performed for all patients using a 3 Tesla MRI scanner with a head coil. Gradient T2 (T2*) and proton-density (PD) weighted spin echo (SE) sequences were carried out in closed and open mouth positions in the oblique sagittal plane (32).

Same MRI slices were selected and compared to the pre- treatment ones. Disc position was measured using kurita et al (33) where a tangent from the lowest edge of the articular eminence (T) to the uppermost edge of the external acoustic pore (P) was drawn (TP). Another line was drawn perpendicular to this tangent touching the posterior border of the articular disc and the point of intersection was marked D. Then distance of TP and TD were measured in millimeters. The disc position was calculated and expressed as TD/TP. (Figure 4)

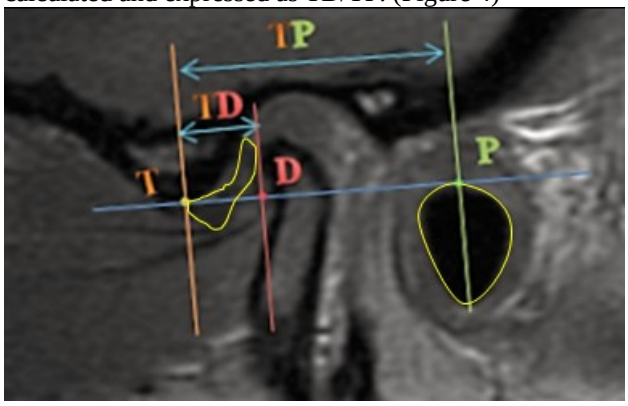

Figure 4: Showing MRI application of Kurita et al method for measuring the articular disc position.

Objective EMG Evaluation

Evaluation of the LPM activity was done using Quantitative EMG interference pattern analysis (IPA) (34) performed by EMG apparatus (Nicolet VickingQuest; Natus, USA).The muscle activity was measured during resisted protrusion. This was done pre-treatment as well as 3 months post-treatment.

Statistical Analysis

Data were collected and entered into the personal computer. Statistical analysis (35) was performed using statistical packages for social sciences (SPSS), version 20 (IBM Corp., Armonk, NY). For categorical variables, chi square test was used to compare between the three studied groups while marginal homogeneity test was used to analyze the significance between the pre and post-treatment in each group. The Kolmogorov-Smirnov test was used to verify the normality of distribution of the quantitative data. For normally distributed quantitative data, parametric tests (ANOVA test and paired t-test) were used. For abnormally distributed quantitative variables, parametric tests (Kruskal Wallis test and Wilcoxon signed ranks test) were applied (35). The 5% was chosen as the level of significance.

RESULTS

Subjective Clinical Evaluation

There was significant improvement in the three studied groups; however, the difference between them was insignificant (p= 0.694) (Table 1).

Table 1: Comparison between the three studied groups according to Helkimo Anamnestic index.

	Ai				
	Pre-treatment		Post-treatment		p_2
	No.	%	No.	%	
Group I	*(n=6)*		*(n=6)*		
0	0	0	2	33.3	0.021*
1	0	0	4	66.7	
2	6	100	0	0	
Group II	*(n=6)*		*(n=6)*		
0	0	0	2	33.3	0.021*
1	0	0	4	66.7	
2	6	100	0	0	
Group III	*(n=6)*		*(n=6)*		
0	0	0	3	50.0	0.033*
1	0	0	2	33.3	
2	6	100	1	16.7	
X^2	3.035				
p	^{MC}p= 0.694				

χ^2, p: χ^2 and p values for Chi square test for comparing between the three groups
^{MC}p: p value for Monte Carlo for Chi square test for comparing between the three groups
p_2: p value for Marginal Homogeneity Test for comparing between pre and post-treatment in each group
*: Statistically significant at $p \leq 0.05$

Objective MRI Evaluation

A significant improvement in the disc position was observed in groups II and III (Figure 5) but there was no significant difference between the three studied groups (p= 0.427) (Table 2).

Table 2: Comparison between the three studied groups according to the articular disc position (mm).

	MRI		
	Pre-treatment	Post-treatment	p_2
Group I	*(n=6)*	*(n=6)*	
Min. – Max.	0.26 – 0.45	0.30 – 0.45	0.178
Mean ± SD	0.34 ± 0.07	0.35 ± 0.07	
Median	0.34	0.35	
Group II	*(n=6)*	*(n=6)*	
Min. – Max.	0.25 – 0.45	0.28 – 0.48	0.003*
Mean ± SD	0.34 ± 0.07	0.38 ± 0.08	
Median	0.34	0.38	
Group III	*(n=6)*	*(n=6)*	
Min. – Max.	0.28 – 0.62	0.28- 0.69	0.010*
Mean ± SD	0.38 ± 0.13	0.43 ± 0.15	
Median	0.34	0.40	
F	0.390	0.902	
p_1	0.683	0.427	

F,p_1: F and p values for ANOVA test for comparing between the three groups
p_2: p value for Paired t-test for comparing between pre and post-treatment in each group
*: Statistically significant at $p \leq 0.05$

Objective EMG Evaluation

There was decrease in the mean of the RMS amplitude of the muscle activity IP reflecting a reduction in the muscle activity. However, that decrease was insignificant in group I but was significant in both groups II and III. Furthermore, there was significant difference between the three groups (p= 0.035) (Table 3).

Table 3: Comparison between the three studied groups according to the EMG RMS Amplitude (μV)

	EMG RMS Amplitude		
	Pre-treatment	Post-treatment	p_2
Group I	*(n=6)*	*(n=6)*	
Min. – Max.	84.0 – 241.0	82.0 – 221.0	0.066
Mean ± SD	147.50 ± 62.21	143.50 ± 57.04	
Median	125.0	124.50	
Group II	*(n=6)*	*(n=6)*	
Min. – Max.	71.0 – 204.0	42.0 – 188.0	0.028*
Mean ± SD	123.50 ± 45.54	70.67 ± 57.65	
Median	108.0	50.0	
Group III	*(n=6)*	*(n=6)*	
Min. – Max.	72.0 – 241.0	31.0 – 204.0	0.028*
Mean ± SD	141.8 ± 71.2	71.50 ± 65.38	
Median	107.0	50.0	
H	0.144	6.690*	
p_1	0.930	0.035*	

H,p_1: H and p values for **Kruskal Wallis test** for comparing between the three groups
p_2: p value for **Wilcoxon signed ranks test** for comparing between pre and post-treatment in each group
*: Statistically significant at $p \leq 0.05$

DISCUSSION

In this study, we investigated the effect of BTX-A as an evolving treatment modality in the management of patients complaining of TMJ pain and clicking associated with DDr. Furthermore, we compared between the use of BTX-A with or without ARA and using ARA as a solitary treatment in the management of the patients with DDr.

ARA is believed to be the appliance of choice to be used in treating patients with DDr, as it could help patients

to avoid progression from TMJ clicking to TMJ locking (17, 19, 20). ARA permits retrodiscal tissue to heal, therefore decreasing TMJ pain and clicking. Gray R. and Al-Ani Z. (36) considered ARA a successful treatment modality in cases of DDr without the need to use invasive methods. These studies showed the efficacy of the short-term use of ARA in alleviating TMD symptoms which goes in accordance to our results.

BTX-A temporary weakens the muscle activity without any systemic effects. Several studies addressed the efficacy of BTX-A in managing TMD of myogenous origin where it was injected in the masseter and temporalis muscles (23, 27, 28). On the contrary, fewer studies investigated its efficacy in cases of internal derangements as DDr (13, 29). Since its close relation to the articular disc, the LPM plays a crucial role in the etiology of the DDr. An uncoordinated muscular activity of LPM would contribute to articular disc instability leading to DDr (9-13).

In our study, 30 U of BTX-A were injected in the LPM, without differentiation between both heads, under guidance of EMG ensuring intramuscular injection which proved to be effective in treating patients with DDr as shown clinically in terms of reduction in TMD pain and cessation of clicking. In addition, improvement in disc position as detected by MRI was obtained from our study. These results are in agreement with Bakke et al (13) and Hassan MA et al (29) studies. Moreover, the reduction in the muscle activity after BTX-A injection in LPM, measured by EMG, associated with the good results obtained clinically and through MRI may support the theory that LPM plays a role in the etiology of DDr. Furthermore, it goes in agreement with Murray et al (12, 37) proposal that both heads of LPM should be regarded as a" system of fibers acting as one muscle, with varying amounts of evenly graded activity throughout its entire range, and with the distribution of activity within the muscle being determined by the biomechanical demands of the task". The results of our study highlight the theory that ID may be caused by imbalance in the LPM activity during mouth opening and closing as proposed by Fujita et al (10) and Manfredini (9).

In view of the results of our work, ARA as well as BTX-A injection to LPM could be considered effective in managing patients with DDr as both provided significant improvement in TMD symptoms.

CONCLUSION

Within the limitations of our study regarding the sample size as well as the short period of evaluation, we can conclude that conservative and reversible treatment modalities including occlusal appliances and pharmacological agents should be considered before any surgical interventions in the management of TMD. Moreover, anterior repositioning appliance is effective in treating patients with disc displacement with reduction; however, Botulinum Toxin Type A with and without anterior repositioning appliance proved to be a more valuable treatment modality in the management of disc displacement with reduction.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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