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Treatment of chronic myofascial pain syndrome associated with parafunctions by use of botulinum toxin type A

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ABSTRACT

Myofascial pain dysfunction syndrome (MPDS) of the temporomandibular joint (TMJ) as a psychophysiological disorder has been developed due to the hyperactivity of mastication muscles. Stress has probably induced parafunction such as bruxism and clenching. The term generally applied for muscle pain and occurred with palpation is "myofascial pain." Diagnosing and explaining the pathology in terms of muscle pain is under research. Few treatment methods have been attained including education, self-care, physical therapy, intraoral appliance therapy, short-term pharmacotherapy, behavioral therapy, and relaxation techniques such as Botox injections on the masseter and temporalis muscles. The purpose of the study is to define the efficacy of the botulinum toxin type A in the chronic masticatory muscle-spasm treatment of elevators muscles to relief the orofacial pain by Helkimo index criteria (a clinical dysfunction index type) usage. The current study has been conducted in a clinical examination with 18 patients including 17 females and one male in with age range of 17-48 with MPDS by using of Helkimo index criteria. The local injection of botulinum toxin type A has constituted an innovative and efficient treatment for chronic facial pain related to hyperactivity of the masticatory muscles. The painful symptoms might be improved in all samples with no reaction to conservative treatment methods and physical therapy. Also, Botox therapy has seemed beneficial in nocturnal bruxism treatment. Another study with more samples is recommended to confirm the outcome of this study.

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INTRODUCTION

The masticatory apparatus has been multiply used in sucking, speaking, cutting, grinding food, and swallowing, therefore, any functional losing related to the pain has been named as masticatory system disorders causing significant distress with severe disabling (Lester W B *et al.,* 2008). Chronic facial pain often presents complex problem management requiring interdisciplinary consults accompanied by multiple therapy modalities. The current study has focused on the treatment of the masticatory system dysfunction. It is more prevalent among women than men. The symptoms of TMD have included a chronic or acute facial pain, tenderness of the masticatory muscles, TMJ pain, TMJ clicking or crepitus during motion, jaw deviation, and functional limitation of jaw opening.

According to the American Academy of Orofacial Pain, TMD is classified into two groups as 1) myogenous TMD related to masticatory muscle disorders, and 2) arthrogenous TMD related to TMJ itself (Buescher JJ, 2007). Also, Research Diagnostic Criteria (RDC) has commonly categorized TMD

into three groups as I) myofascial TMD, II) disc displacement, and III) other TMD comprising arthralgia, osteoarthritis, and osteoarthrosis (Dworkin SF and LeResche L, 1992). For the majority of TMD patients seeking medical treatment, a group I and group II RDC/TMD are mostly presented. The aetiology of TMD is difficult for defining, moreover, few more parameters might have great role in causing TMD, say trauma, adverse loading of the masticatory system, parafunctional habits, systemic factors (such as hormones), anatomical factors, and also psychosocial factors (Poveda Roda R *et al.,* 2007; Lobbezoo F *et al.,* 2004; Abenavoli FM et al, 2003). Few patients have complained from rapid eye movements syndrome (REMS) associated with masticatory muscles hyperactivity characterised by parafunction such as nocturnal clenching and\or nocturnal bruxism, tension headache at the temporal area, nightmares, teeth sensitivity and tenderness, orofacial pain, and pain in masseter and temporalis muscles on palpation. All the patients have suffered from stress disrupted sleeping and keeping in the REM stage led to parafunctional habits during sleep. Accordingly, stress has induced parafunction like clenching and bruxism. On the other hand, emotional cases like anxiety might elicit a variety of oral habits such as lip-biting or cheek-biting, teeth clenching or grinding, nail-biting, and general masticatory muscle tension (Laskin D M, 1969; Westling L, 1988), making resistance to few treatments of this condition including occlusal splints (Dao TT and Lavigne G J, 1998; Raphael K and Marbach JJ, 2001), physiotherapy (Nicolakis P, 2002), behavioral and physical treatments (De Laat A *et al.,* 2003), and drugs (Dionne RA, 1997; Manfredini D et al. 2004).

The common therapy is muscle relaxation, thereafter, botulinum toxin (BTX-A) injections for the most symptomatic elevator muscles have been selected based on special cases injecting to masseter and temporalis muscles bilaterally. The symptoms of orofacial pain normally appear in the elevator muscles, closing the mouth during clenching and bruxism. Moreover, the chronic muscle hyperactivity has produced muscular fatigue with myospasm radiated to the orofacial area to cause myofascial pain dysfunction syndrome. Clostridium botulinum is a Gram-positive anaerobic bacterium produces 7 various toxins like serotype A. BTX-A binds the presynaptic membrane of the motor end plate and blocks acetylcholine releasing with no affects either on normal conduction or acetylcholine synthesis and storage (Tsui JKC, 1996; Jankovic J and Hallett M, 1994). The toxin is internalized into the presynaptic cholinergic nerve terminals inhibiting muscle contraction and modifies spindle afferent discharge, thus acting as a muscular relaxant through the acetylcholine release inhibition (Harvey AL., 1990; Borodic G *et al.,* 1996; Ahnert-Hilger G and Bigalke H, 1995; Rosales RL *et al.,* 1996). BTX-A for its therapeutic use in humans is approved by the United States Food and Drug Administration (FDA) in 1989 -2000, followed by extensive use in few other cases (Scott AB *et al.,* 1985; Carruthers J and Carruthers A, 1998; Matarasso SL, 1998; Andrews CN *et al.,* 1999; Brisinda G *et al.,* 1999). The action starts from a few days to two weeks, while BTA has corresponded to the period of functional denervation in (3-4) months. Isometric-force measurement in dogs has indicated a 10-week duration of BTA effecting (Childers MK *et al.,* 1998).

The current research aims to test the role of BTX-A as a treatment modality for chronic myofascial pain dysfunction syndrome caused by spasm of masticatory muscles through the Helkimo index criteria. Also, the results of pretreatment after two weeks - one month of injections have been recorded to measure the efficacy of Botox treatment.

PATIENTS AND METHODS

Patient's selection

18 patients (17 female-one male) from the oral department in dentistry college of Kerbala University in Kerbala/ Iraq have been gathered in years of October 2017 - November 2018. The age range is 20 - 53 years (mean age 32 years). Samples have been diagnosed with chronic myofascial pain dysfunction syndrome. On the other hand, masticatory muscles hyperactivity has also been diagnosed on visible symptoms such as grinding/ bruxing sounds during sleep across the past six months for at least five nights a week reported by their immediate family members or self-declaration; Subsequently, at least one of the following adjunctive criteria has occurred 1) tooth wear or shiny spots on restorations and present of abfractions, 2) masticatory muscle fatigue or pain in the mornings, 3) masseteric hypertrophy upon digital palpation, and 4) symptoms of rapid eye movement syndrome (REMS).

Myofascial pain of the masticatory muscles has been diagnosed based on the clinical dysfunction index with guidelines for TMJ dysfunction syndrome (as the second type of Helkimo Index). All samples have suffered from long sleep disturbance led to REM syndrome with nocturnal clenching and bruxism, temporal tension headache, nightmares, teeth sensitivity/ tenderness, and orofacial pain. Accordingly, none has responded appropriately to muscles relaxant medicines, relaxing techniques or physical therapy led to BTX-A injections for elevator masticatory muscles (superficial masseter and

temporalis muscles) responsible for most muscular hyperactivity and myospasm eliciting the most symptoms of TMJ dysfunction syndrome and orofacial pain. Limitations of the current study are as follows: treatment history recording for bruxism or TMD in one month before the study, presence of neuromuscular pathologies have prevented the botulinum toxin using (i.e., myasthenia gravis), reporting of hypersensibility to Clostridium botulinum type A neurotoxin, active inflammation or infection in the injection site, pregnancy and breastfeeding, and multiple sclerosis.

METHODS

Samples are injected of BTX-A (50 units) by intramuscular injections of elevator muscles to close the mouth and doing the parafunction as 15 units for right and left superficial masseter muscles and 10 units for anterior temporalis muscles for each side equally. Dilution of BTX-A vial with 1.75 ml of normal saline has been injected to the masseter muscle (15 units) to each side at four points in a square figure on the angle of mandible while asking the patients to clench their teeth to check the inserted portion of the superficial masseter muscle. Accordingly, the masseter muscles have equally received 30 units of BTX-A due to its potency and activity in the mouth which is closed during the nocturnal parafunctional habits compared to the temporalis muscle which is equally received 20 units of BTX-A in 3 injections in a triangle shape on its top toward the eyebrow. The injection points at the anterior portion of the temporalis muscle and its function have mainly elevated the mandible. By repeating the injections to the other side, 50 units BTX-A has been injected to each patient by using subcutaneous syringe of insulin injection in one session. Patients are motivated and instructed prior to the injections about the sleeping position (anterior pelvic for first night), avoiding any press on the injections areas, in case of any allergy symptoms try to inject the hydrocortisone 200 mg with antihistamine while calling the emergency, difficulty in chewing for first two weeks and following the soft diet. All patients have pretreatment data of Helkimo criteria, treatment sessions of every two weeks and one month to write the case sheet of Helkimo criteria (figure 4), analyzing of the BTX-A treatment results to relief the pain of chronic masticatory myospasm of TMJ.

RESULTS

The results of this study are obtained and analyzed from the recording data of three injection sessions of BTX-A by use of Helkimo criteria as Table. 1 illustrating the range of mandibular motion is significantly 0.016, the Muscle tenderness during palpation is significantly 0.0005, the TMJ function impairment is significantly 0.003, TMJ pain during palpation is significantly 0.001, the pain during mandibular movements is significantly 0.002, and the summation of scorings of Helkimo criteria of is also significantly 0.0005.

Table 1: General Comparison Between Visits (Pretreatment, After 2 weeks & After 1 month)

Criteria of Helkimo index	Sig.
Range mandibular motion	0.016
Muscle tenderness during palpation	0.0005
TMJ function impairment	0.003
TMJ pain during palpation	0.001
Pain during mandibular movements	0.002
Summation	0.0005

Multiple comparisons have been performed by Tukey HSD test and Games-Howell test (Table 2) illustrating that the range of mandibular motion in Tukey HSD test between the pretreatments and after two weeks of treatment is significantly 0.032, and one month after treatment is 0.032, however, there is no significant ratio between the two weeks and after 1 month of treatment (1.000). Muscle tenderness during palpation in Tukey HSD test has shown significant ratio only between pretreatment and after two weeks as 0.0005, also the significant ratio of 0.0005 between pretreatment after 1 month, however, there is no significant ratio between two weeks and after 1 month of treatment (0.522). TMJ function impairment in Games-Howell test has shown the significant ratio between pretreatment and both two weeks (0.041) and one month (0.025) after treatment, while the comparison of the two weeks and one month after treatment has shown no significant ratio (0.926). TMJ pain during palpation in Games-Howell test has shown the significant ratio between pretreatment and both two weeks (0.022) and one month (0.040) after treatment, but the comparison of the two weeks and one month after treatment has shown no significant ratio (0.714).

The pain during mandibular movements in Games-Howell test has shown the significant ratio between pretreatment and both two weeks (0.028) and one month (0.009) after treatment, however, the comparison of the two weeks and one month after treatment has shown no significant ratio (0.765). To sum up, the comparison of pretreatment, two weeks and one month after treatment has shown significant ratios of 0.0005 & 0.0005, while the comparison of the two weeks and one month after treatment has shown no significant ratio (0.812). The code of Helkimo index (Table 3 & Figure 1-6) has represented the number and ratio of each clinical dysfunction index code if clinically is symptom free, mild dysfunction, moderate dysfunction, and severe dysfunction based on the summary scores of Helkimo criteria from five

Table 2: Multiple Comparisons

(I) Treatment	(J) Treatment	Mean Difference (I-J)	Std. Error	Sig.
Range mandibular motion "Tukey HSD Test."				
Pretreatment	After 2 weeks	1.056*	0.405	0.032
Pretreatment	After 1 month	1.056*	0.405	0.032
After 2 weeks	After 1 month	0.0005	0.405	1.000
Muscle tenderness during palpation "Tukey HSD Test"				
Pretreatment	After 2 weeks	3.222*	0.457	0.0005
Pretreatment	After 1 month	3.722*	0.457	0.0005
After 2 weeks	After 1 month	0.5	0.457	0.522
TMJ function impairment "Games-Howell Test"				
Pretreatment	After 2 weeks	0.722*	0.278	0.041
Pretreatment	After 1 month	0.778*	0.275	0.025
After 2 weeks	After 1 month	0.056	0.148	0.926
TMJ pain during palpation "Games-Howell Test"				
Pretreatment	After 2 weeks	1.222*	0.415	0.022
Pretreatment	After 1 month	1.111*	0.420	0.040
After 2 weeks	After 1 month	0.111	0.141	0.714
Pain during mandibular movements "Games-Howell Test"				
Pretreatment	After 2 weeks	1.556*	0.568	0.028
Pretreatment	After 1 month	1.833*	0.567	0.009
After 2 weeks	After 1 month	0.278	0.397	0.765
Summation "Games-Howell Test"				
Pretreatment	After 2 weeks	7.778*	1.277	0.0005
Pretreatment	After 1 month	8.500*	1.422	0.0005
After 2 weeks	After 1 month	0.722	1.172	0.812

* The mean difference is significant at the 0.05 level

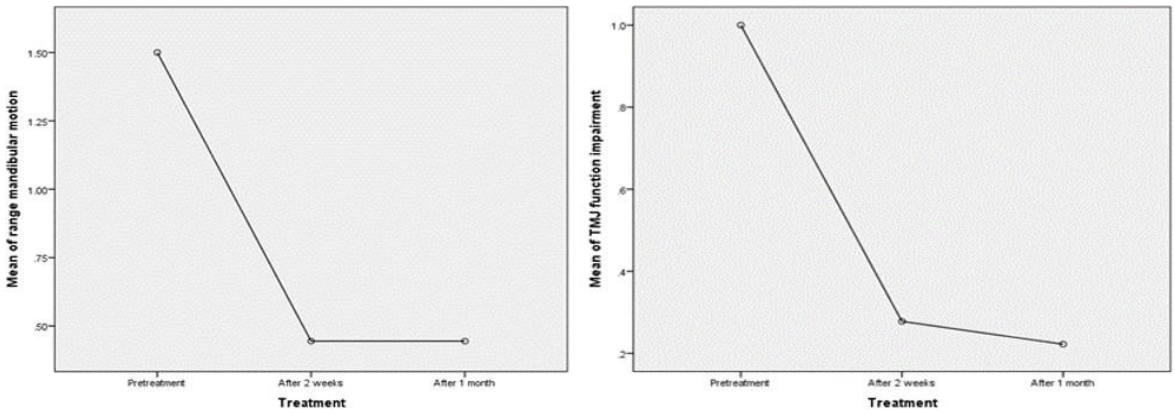

Figure 1: Range mandibular motion, TMJ function impairment

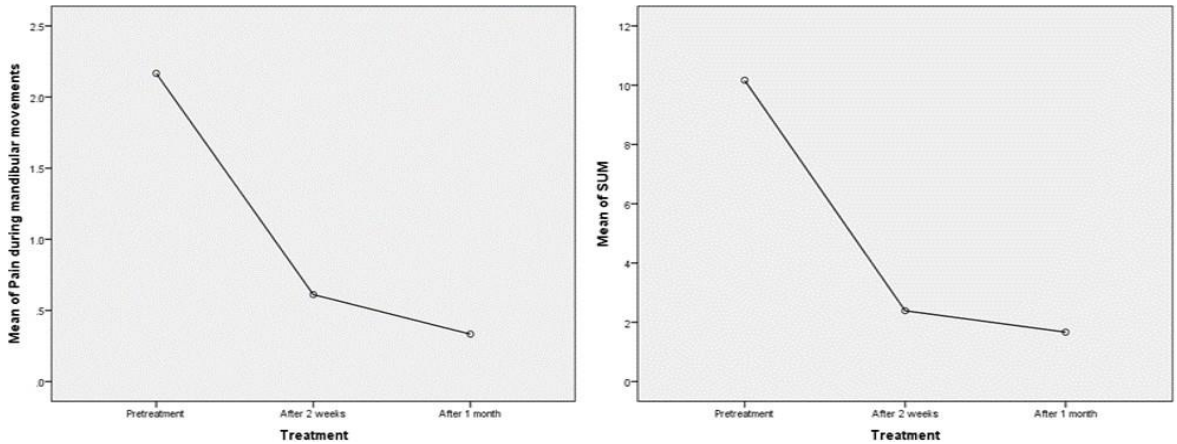

Figure 2: Pain during mandibular movements, Summation

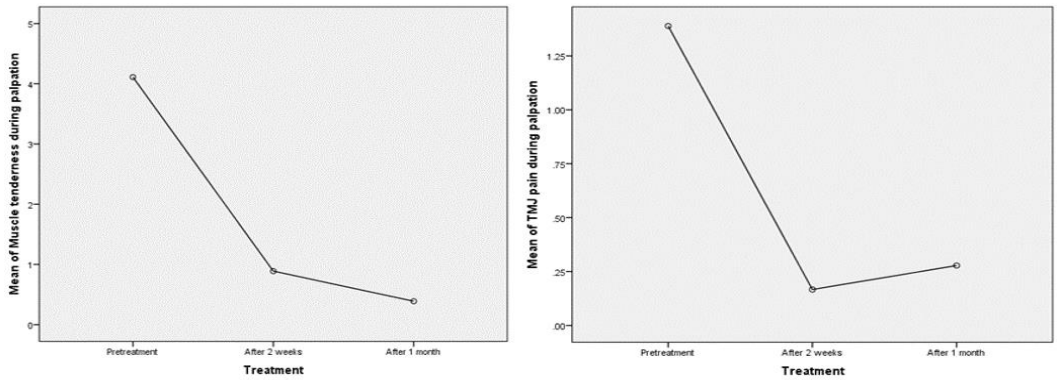

Figure 3: Muscle tenderness during palpation, TMJ pain during palpation

Table 3: The code of index Treatment

		Pre treatment	After 2 weeks	After 1 month	Total
The code of index	Clinically symptom-free	0	4	10	14
		0.0%	28.6%	71.4%	100.0%
	Mild dysfunction	3	13	7	23
		13.0%	56.5%	30.4%	100.0%
	Moderate dysfunction	7	0	0	7
		100.0%	0.0%	0.0%	100.0%
	Sever dysfunction	8	1	1	10
		80.0%	10.0%	10.0%	100.0%
Total		18	18	18	54
		33.3%	33.3%	33.3%	100.0%

UNIVERSITY OF KERBALA / COLLEGE OF DENTISTRY case no. .....

Patient's Name: ..... Age: ..... Gender: .....

Address: ..... Occupation: .....

Chief complain.....

.....

History of present illness .....

Habits:- day & nocturnal bruxism or clenching , nail-object biting , lip-cheek biting , prolong gum chewing , habitual unilateral chewing?.....

Clinical examination:-

Obvious abnormal occlusion as acute or chronic malocclusion, poor crown & bridge, High spots, poor CD /PD & other?.....

.....

Temporal headache .....

1- Helkimo index (clinical dysfunction index type):- According to dysfunction scores (0-5). (pretreatment)

a- Range of mandibular motion (degree of mouth opening) ,.....( )

b- TMJ function impairment ,.....( )

c- Muscle tenderness during palpation ,.....( )

d- TMJ pain during palpation ,.....( )

e- Pain during mandibular movements ,.....( )

The sum of a+b+c+d+e (0-25): ( ) / The code of index: ( )

2- Is there is any changes in signs & symptoms of Helkimo index after two weeks of treatment:-

a-.....( )

b-.....( )

c-.....( )

d-.....( )

e-.....( )

The sum of a+b+c+d+e (0-25): ( ) / The code of index: ( )

3- Is there is any changes in signs & symptoms of Helkimo index after one month of treatment:-

a-.....( )

b-.....( )

c.....( )

d-.....( )

e-.....( )

The sum of a+b+c+d+e (0-25): ( ) / The code of index: ( )

Figure 4: Case Sheet

questions illustrated in the patient's case sheet (Figure 4).

Index code has indicated that there is no clinically symptoms free (CSF) in the pretreatment stage, therefore, all patients are diagnosed well and complained from the chronic myofascial pain syndrome, also after two weeks of treatment, there are four patients cured and recorded CSF; Thus after one month of treatment, index code records 10 CSF while the index code has recorded three cases of mild dysfunction in pretreatment stage, 13 cases in two weeks after treatment, and seven cases in one month after treatment. The index code records seven cases of moderate dysfunction in the pretreatment stage while there are no cases of moderate dysfunction in two weeks and one month after treatment. The index code records eight cases of severe dysfunction in the pretreatment stage while there is only one case recorded of severe dysfunction in the two weeks, and one month after treatment.

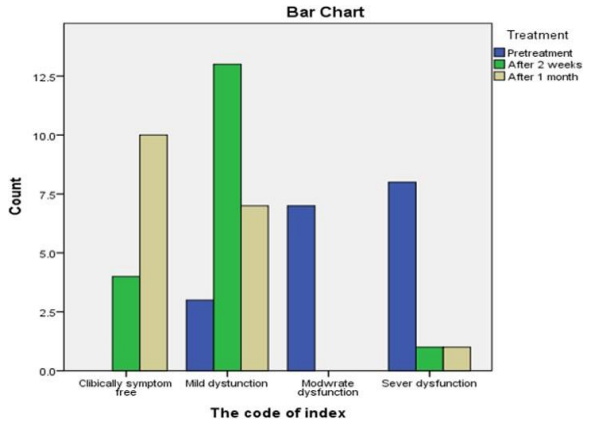

Figure 5:

DISCUSSION

The most common treatment approach to myofascial pain of masticatory muscles is according to reversible and conservative symptomatic therapeutic modalities like occlusal splints, physiotherapy, behavioral and physical treatments and drugs. Considering the studies, it's hypothesized that botulinum toxin has mightily presented an alternative option avoiding the prolonged treatment with occlusal splints or drugs (Borodic GE and Acquadro MA, 2002). Severe clenchers and bruxers injections in the masseter and temporalis muscles with botulinum toxin in an open-label prospective trial have reported significant improvement in symptoms and minimal adverse effects (Mense S, 2004). The effecting of BTX-A treatment has lasted 5 months while should be repeated to give its paralytic effect on the muscles by inhibiting the acetylcholine releasing at the neuromuscular junction (Guarda-Nardini *et al.,* 2008).[29] BTX-A has also been proposed in chronic parafunctions treatment, so that the elevator's muscles have reduced the number of sleeping-episodes related bruxism and clenching (Lee SJ *et al.,* 2010).

BTX therapy for TMDs has been pioneered (Freund B and Schwartz M, 1998; Freund B *et al.,* 1999). Few more TMD cases of clenching, bruxism, or parafunction of the jaw have hypothesized that the inhibition of muscle activity by paralysis has mightily improved the symptoms of TMD. Freund et al. (1999) have enrolled 15 subjects with no specified TMDs, treated with 150 units BTX-A in bilateral masseter and temporalis muscles which have resulted in a significant improvement in pain relief, function, mouth opening, and tenderness for the patients. In contrast, TMJ improvement has been performed by injecting of 50 units BTX-A for 18 subjects indicating a significant ratio in mandibular motion, muscle tenderness during palpation, TMJ function impairment, TMJ pain during palpation, and pain during mandibular movements (Table 1), therefore, align with other studies, 90% to 95% response rate to BTX-A injection in patients with chronic myofascial pain syndrome have been confirmed (Jankovic J and Brin MF, 1991; J. De Andrés *et al.,* 2003; Jens J. von Lindern *et al.,* 2003). Considering the influence duration of BTX-A (4-5 months), injections have to be repeated, even if it is problematic due to the immunogenic of botulinum neurotoxins (Zuber M *et al.,* 1993). The results have also indicated that all patients are satisfactorily responded in the second visit after BTX-A injection in terms of all symptoms of chronic myofascial pain syndrome based on Helkimo criteria index of the pretreatment visits, and also indicated an orofacial pain reduction related to the masticatory muscles spasm due to parafunctions, such as clenching and bruxism requiring no extra injection-dose of BTX-A after the first injection. Accordingly, the results have significantly confirmed the patients' willingness and relief in the orofacial pain, temporal head, teeth tenderness, and mandibular movement limitations. However, BTX-A is not the first treatment option for most masticatory muscle pain disorders.

Meanwhile, BTX-A has not permanently relaxed muscles, so removed from the definitive therapy. Anytime the clinician can eliminate the aetiology of the pain disorder; it should be done provoking to manage any disorders. Respectively, acute myalgic conditions such as protective co-contraction and local muscle soreness are not candidates for BTX-A injections. Even myofascial pain has to be managed firstly by techniques such as occlusal splints, physiotherapy, behavioral and physical treatments, and drugs. In case of any muscle pain persistence even after initial therapies, BTX-A might be regarded.

Furthermore, there is a growing support in the management of chronic myofascial pain with botulinum toxin injections (Gobel H *et al.,* 2006; Kamanli A *et al.,* 2005; Royal MA, 2003; Lang AM, 2003; De Andres J *et al.,* 2003; Lang AM, 2003; Porta M, 2000; Cheshire WP *et al.,* 1994; Freund B *et al.,* 2000; Daelen B *et al.,* 1997; Ivanhoe CB *et al.,* 1997; Moore AP and Wood GD, 1994; Moore AP and Wood GD, 1997; Sankhla C *et al.,* 1998). Contrary, few types of research have revealed that botulinum toxin injections have no more influence than placebo injections (Ojala T *et al.,* 2006; Graboski CL *et al.,* 2005). Epidemiological, clinical, and test evidence in terms of gender variation in the incidence of musculoskeletal pain have indicated that pressure pain thresholds are constantly lower in women than men showing that the decrease is a matter of sex and a raised sensitivity to deep pains which has made women more vulnerable to MPS (Rollman GB and Lautenbacher S, 2001). Thus, the results have shown both the safety features of this technique and the low adverse effects ratio recorded in 11 patients complaining of the difficulty in chewing the hard foods during the first 10 days after BTX-A injection led to soft diet instruction in this period. Subsequently, in this study, no hypersensitivity, numbness, and facial disharmony due to facial muscles paralysis had been reported. The curbs of this study have comprised a small sample size, lack of data on temporal headache and gender-variations. The study also has few design confinements affecting the results assessment, especially because of no control group to be compared with the group treated by BTX-A. The current study has tried to provoke the scientific community to pursue further research in chronic myofascial pain syndrome treatment.

CONCLUSIONS

According to the results, BTX-A therapy might be a valuable alternative in pain treatment of MPS from both efficacy and safety matter. The local injection of botulinum toxin type A is an effective treatment for chronic facial pain related to hyperactivity of the masticatory muscles. There is an improvement in pain symptoms in all the patients with no response to traditional treatments and physical therapy. Botox therapy has been promised in the treatment of masticatory pain associated with nocturnal bruxism and clenching regardless of its high costs and repeated injections necessity. Further studies with greater sample numbers might confirm the results obtained in this study.

Conflicts of interest

The authors have declared no conflict of interests.

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Consent

Patient consent has been obtained for the medico-legality reason.

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