Section A-Research paper

TO COMPARE THE EFFICACY OF BOTULIUM TOXIN TYPE A(BTX-A) THERAPY, AND A COMBINATION OF BOTH IN THE MANAGEMENT OF MYOFASCIAL PAIN DYSFUNCTION SYNDROME

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ABSTRACT

Background: Myofascial Pain Dysfunction Syndrome is the most prevalent cause of orofacial pain and a subset of temporomandibular disorders. Treatment of MPDS necessitates deactivation of MTrPs, restoration of normal muscle length, and elimination or correction of the conditions that caused or perpetuated the TrPs in the first place. Our study aims to compare the efficacy of Botulinum Toxin type A therapy, Conservative therapy, and their combination in the management of MPDS

Methods: Using simple random sampling with a random number generator, 15 patients diagnosed with MPDS were assigned to three groups. Group A received conservative treatment; group B received Botulinum Toxin A injection, and group C received both. The observations were based on pain assessment using Visual Analog Score, mouth opening in millimeters, and overall improvement.

Results: The mean VAS score was significantly improved in group C, a baseline was 7.0 which was reduced to 1.8 at the end of the 12^{th} week. However, the mean difference in VAS score between the three groups was not found to be statistically significant. (p=0.07) The mean mouth opening improved in all groups. A significant improvement was seen in group C which was 26.0 at baseline and significantly increased to 39.0 by the end of the 12^{th} week. The mean difference in mouth opening between the 3 groups was found to be statistically significant. (p=0.03)

Conclusion: Based on the evaluation of parameters, Group C improved significantly in pain and mouth opening when compared to other groups, with no adverse effects.

Keywords: Myofascial pain dysfunction syndrome, Myofascial Trigger points, Botulinum Toxin type A.

INTRODUCTION

Temporomandibular disorders (TMDs) are a cluster of conditions that involve the temporomandibular joint (TMJ), muscles of mastication, and musculoskeletal system of the head and neck. TMD patients complain of pain in the preauricular region, the TMJ, masticatory muscle tenderness, restriction in mouth opening or mandibular deviation, and TMJ sounds (clicking, popping, crepitus) during mandibular function. Other typical issues include headaches, radiating pain to the neck and ear, tinnitus, or fullness in the ear. (1,2)

Myofascial Pain Dysfunction Syndrome (MPDS) is a subset of TMD and one of the most common causes of pain in the head and neck region. It is a psychophysiological illness that affects the masticatory muscles, causing pain, limitation in jaw motions, joint sounds, jaw deviation when the mouth is closed and opened, and tenderness during palpation of masticatory muscles. (3) MPDS was previously thought to be an inflammation of the fibrous tissues that surround the stomatognathic system's ligaments, tendons, muscles, and periosteum. However, it is now more widely characterized as "dysfunction of the masticatory and its associated muscles. (4) Usually it is unilateral and, during the examination, tenderness in one or more masticatory muscles or their tendinous attachments can be felt. Headache is a prevalent symptom of MPDS, Muscle spasms or tension headache is the only type of headache that the syndrome can cause directly or indirectly, with other types being coincidental observations. MPDS is thought to be a stress disorder. Muscle fatigue and spasm are thought to be caused by an increase in muscle strain, which, when coupled with non-functional habits such as teeth clenching or grinding, results in discomfort and dysfunction. (5)

Travell and Rinzler (1952) described the existence of MTrPs, a characteristic feature of MPDS. (6) MTrPs are hyperirritable nodules that patients frequently characterize as "knots" that are positioned in a taut band of skeletal muscle or the muscle fascia that, when compressed, can cause typical referred pain, motor dysfunction, and autonomic phenomena. (7)

The principles of MPDS management include recognizing symptoms, which leads to an accurate diagnosis, followed by suitable treatment. Based on the multifactorial origin of such disorders, treatment frequently entails more than one modality to provide complimentary results, such as counseling, pharmacological therapy, and physical therapy. Long-term effects are achieved with treatments such as exercise therapy, anti-inflammatory medicines, local anesthetic injections, stretching therapy, occlusal splint, psychotherapy, ultrasound, biofeedback, and transcutaneous nerve stimulation (TENS), but each treatment modality has its own set of advantages and disadvantages. (6)

Botulinum toxin (BTX) injections can be given into the masticatory muscles if conventional therapies fail. It is a neurotoxin produced by the bacterium clostridium botulinum. This neurotoxin particularly inhibits acetylcholine (ACh) release in the

presynaptic neuromuscular junction causing flaccid paralysis. It is used to treat trismus, bruxism, masticatory muscle myalgia, TMJ problems, and muscular hypertrophy by injecting it into the masticatory muscles. (8)

Many traditional techniques share a common goal: muscular relaxation. As a result, BTX-A can stop muscular contraction for a longer period, providing even more relief by selectively weakening painful muscles. It may also halt the pain process long enough for a long-term reaction to develop, such as the ability to engage in kinds of physical exercise required for long-term healing. (9)

This study was planned was to compare the efficacy of a combination of conservative treatment and BTX-A injections in the treatment of MPDS to conservative treatment and BTX-A injections given separately.

MATERIALS AND METHODS

Study population and design:

The study enrolled a total of 15 patients who reported to the Department of Oral and Maxillofacial Surgery in JSS Dental College and Hospital/ Dental Unit of JSS Medical College and Hospital, JSS University, Mysore diagnosed with MPDS. For each patient, a complete history was taken that included the chief complaint, relevant prior medical history, drug history, allergy, and personal history. They were assessed both symptomatically and clinically. Patients included were over 18 years of age with unilateral or bilateral MPDS and who were willing to give their consent for participation in the study. Patients were excluded as study subjects if they had a history of significant allergic reactions to NSAIDS or BTX-A, active inflammation or infection at the proposed injection site, any chronic degenerative neuromuscular disorder, pregnancy or lactating mothers, and who were below 18 years of age.
After getting diagnosed with MPDS patients were randomly assigned to study groups using simple random sampling with a random number generator. Group A: Conservative management group, Group B: BTX-A Group, Group C: Combination Group

Ethical approval was obtained from the institutional ethical committee before starting the study (JSSDCH IEC Research Protocol No: 43/2019)

Patients in group A (*n*=5) received conservative therapy that included anti-inflammatory medication, a muscle relaxant, and a soft splint (in cases of parafunctional habit). They were asked to perform jaw exercises and hot fomentation.

Patients in group B (*n*=5) received BTX-A injections into the trigger points of masseter and temporalis. Anesthetic cream was applied before the injection to make the patients

more comfortable during the treatment. Typically, 3-5 injections were administered on one side.

Patients in group C (*n*=5) received BTX-A injections along with conservative therapy.

Botulinum Toxin – A Injection Procedure:

BTX A is kept frozen in a vial at 2 - 4° C until ready to use. Following the manufacturer's instructions, the drug was dissolved in 0.9% preservative-free normal saline. According to the trigger points, the main masticatory muscles, masseters, and temporalis muscles were injected. Before the injection, Lidocaine Hydrochloride Jelly was applied to the trigger points area. Alcohol wipes and dry sterile gauze sponges are used to prepare the skin. Aspiration was done before injecting the toxin. 50 IU BTX-A was dissolved in 1.0 milliliters of sterile saline solution (0.9 percent) at room temperature to make the BTX-A solution. It was carried out right before the injection. Injections were given with an insulin syringe with a hypodermic needle. The palpatory examination was done to identify trigger points. Patients were instructed to clench their jaws. In a single session, 30-50 units were injected into one side of each patient. 10 U in the lower masseter near the angle and 10 U 1cm in front and above the first injection site, which usually corresponds to MTrPs. To avoid frontalis muscle paresis, the temporalis muscle was injected 1 cm behind the hairline, followed by 1 cm behind it. (Fig 1)

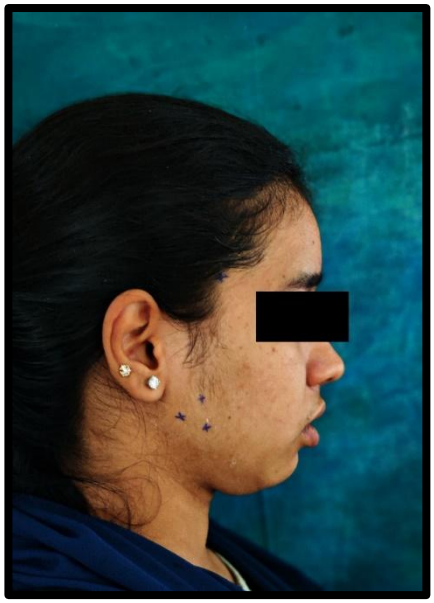

Fig 1: Marking of the trigger points

The patients were followed up for 12 weeks. The evaluation was done at (post-injection) 1st week, 2nd week, 6th week, and 12th week.

At all follow-ups, the requirement for any additional analgesics was noted. If an additional tramadol paracetamol combination is required by the patient in group A and Group C

Observations were be based on -

1. pain assessment using VAS
2. mouth opening in mm
3. overall improvement in symptoms

Statistical analysis:

Data were analyzed using Excel (Microsoft) and SPSS (v.22) software. Non-parametric tests i.e., Kruskal Wallis test and Chi-square test were used for the analysis.
A value of p <0.05 was regarded as significant.

RESULTS:

Our study included 15 patients. The study population was predominantly female in which there were 9 female patients (60%) and 6 male patients (40%) with a mean age of 24.0 in group A, in group B, 33.0, and 33.8 in group C, ranging from 19 to 58 years. (Fig 2)

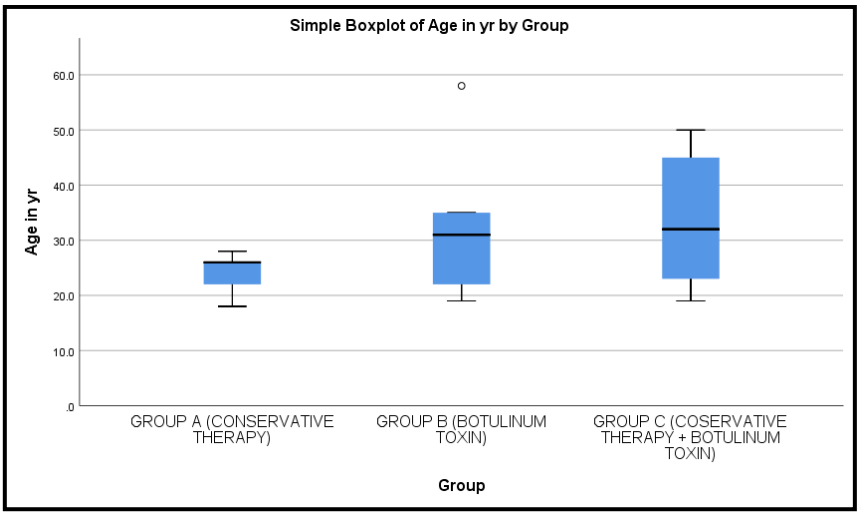

Fig 2: **Age distribution in Group A, Group B, and Group C**

Fonseca Anamnestic Index (10,11) was used for evaluation of myogenic TMD and all patients answered the questions. No significant masticatory muscle hypertrophy was observed in any case. Bilateral involvement of muscles was noted in 2 patients, in group

A (40%), 2 in group B (40%), and one in group C (20%). Out of 15 patients, 3 (20%) had the parafunctional habit and significant improvement was noted in group C as compared to other groups. The masseter muscle was the most commonly injected (100%) in all the groups, whereas 2 patients in group A (40%), 2 in group B (40%), and 3 in group C (60%) received injections in the temporalis muscles. (Table 1)
The primary outcome variables were improvement in pain and an increase in mouth opening.

		Group					
		GROUP A (CONSERVATIVE THERAPY)		**GROUP B (BOTULINUM TOXIN)**		**GROUP C (CONSERVATIVE THERAPY + BOTULINUM TOXIN)**	
		Count	Column N %	Count	Column N %	Count	Column N %
Masseter	Yes	5	100.0%	5	100.0%	5	100.0%
Temporalis	No	3	60.0%	3	60.0%	2	40.0%
	Yes	2	40.0%	2	40.0%	3	60.0%

TABLE 1: affected muscles in Group a, Group b, and Group c

Pain assessment:

The mean VAS pain scores at baseline, 1st week, 2nd week, 6th week, and 12th-week post-treatment are shown graphically in Fig. 3. Patients in group A had a mean score of 6.0 at the baseline which decreased to 3.2 by the end of the 12th week. (p=0.001)
In group B, the mean score was 7.0 at the baseline which decreased to 2.6 by the end of the 12th week. (p=0.001) and in group C, the mean score was 7.0 at the baseline which decreased to 1.8 (p=0.001). However, the mean difference in VAS scores between the three groups was not found to be statistically significant. (p=0.07). There was a reduction in pain in all the groups. Complete resolution of pain was noted in some patients. A significant decrease in VAS scores was noted in group C. Patients in groups B and C reported a reduction in headaches as well after the BTX-A injections.

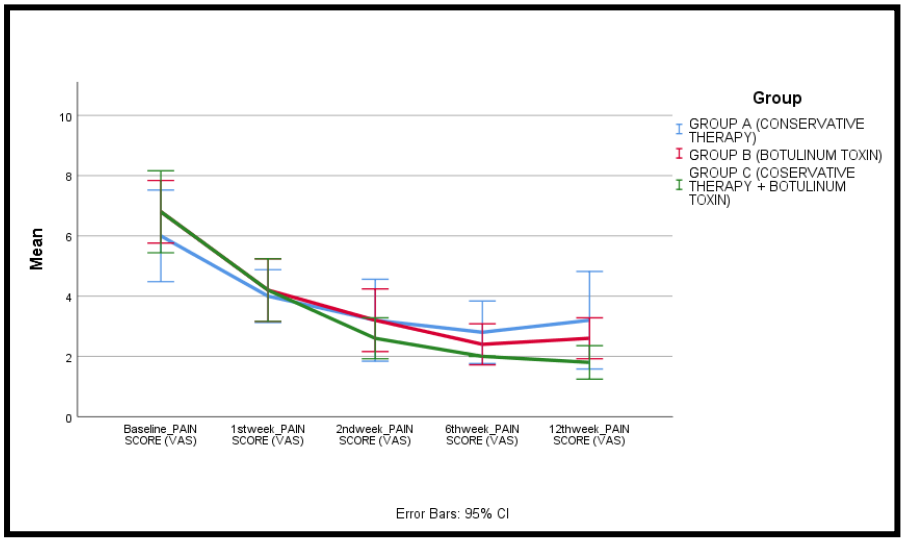

Fig 3: **Improvement in pain at different intervals**

Mouth opening:

The mean improvement in mouth opening at baseline, 1st week, 2nd week, 6th week, and 12th-week post-treatment are shown graphically in Fig. 4**.** Patients in group A had a mean mouth opening of 31.2 at the baseline which increased to 36.0 at the 6th week. It decreased to 35.0 at the end of the 12th week. (p=0.002)**.** In group B the mean mouth opening at baseline was 33.8 which increased to 40.6 at the end of the 12th week. (p=0.002)**.** In group C, the mean mouth opening at baseline was 26.0 which increased to 39.0 at the end of the 12th week. (p=0.002). The mean difference in mouth opening between the 3 groups was found to be statistically significant. (p=0.03) Mouth opening increased in all groups; however, it was significant in Group C when compared to the other groups.

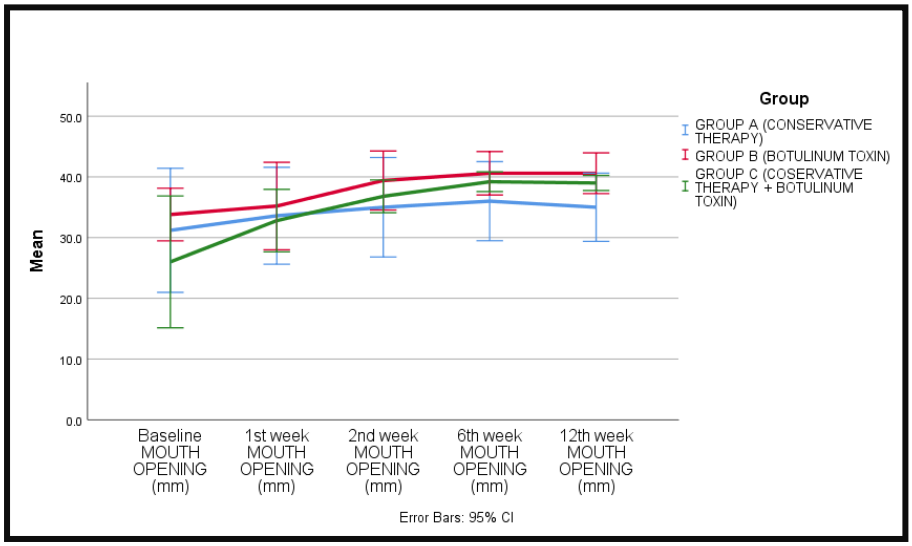

Fig 4: **Improvement in mouth opening in Group A, Group B, and Group C at different intervals**

DISCUSSION:

For decades, myofascial pain has been a source of fascination and consternation. The name "myofascial" came about as a result of the belief that both muscle and fascia are likely to play a role in the symptoms. (12) MPDS has a multifactorial origin, and understanding of the likely etiological variables has improved over time. The connection between muscular dysfunction and MPDS is a two-sided problem, with each side affecting the other. It is caused by muscle malfunction, and it impairs masticatory movements. (13)

Otolaryngologist James Costen in 1934, described a set of conditions centered on-ear and TMJ resulting in the first nomenclature of Costen syndrome. (14) In 1952, Travell and Rinzler speculated that pain could be caused by skeletal muscle spasms. They labeled these painful sites as "Trigger areas," which were associated with pain, spasm, tenderness, and dysfunction. (15) Schwartz in 1959 (16) introduced the term myofascial pain dysfunction syndrome, which is characterized by clicking, tenderness in the muscles of mastication, pain in the TMJ area, and restricted mouth opening. He claimed that emotional stress was a major contributor to clenching and grinding tendencies, which led to muscle spam and occlusal abnormalities. In 1959, Shore first used the term temporomandibular dysfunction syndrome. (17,18) A major development in understanding the MPDS occurred when Laskin 1969 put forward his

psychophysiological theory. He proposed that some cases of MPDS may be caused by mechanical factors that produce muscular overextension or contraction. Chronic oral behaviors such as clenching or grinding of the teeth are the most prevalent cause of muscular fatigue. An irritating dental irritant such as inadequately occluding restoration or an overhanging border might initiate these habits as a method of relief. Rather than occlusal or mechanical issues, Laskin's theory is based on emotional aspects. (19)

Women are three to five times more likely than men to be affected by MPDS. The age range of 20 to 40 years appears to have the highest incidence. (20) It is more common in young unmarried females with a married-to-unmarried ratio of 1:2. (17) There is a female predominance in our study as well (60%).

MPDS, like many other musculoskeletal disorders, can be managed but is difficult to fully cure**.** The goal of the initial treatment should be to return the joint to its previous state of health. Several simple yet effective things can be done at home to reduce muscle fatigue, spasm, and pain, increase mandibular mobility and restore good masticatory function. These include a soft diet, limiting jaw movements, avoiding parafunctional habits, and using heat and massage. (20) There are two types of supportive therapy: a) Those whose goal is to alleviate pain. It entails both pharmacologic and physical therapy, b) Those aimed at resolving dysfunction, such as splint therapy. (21)

The purpose of this study was to find out whether conservative treatment for MPDS when coupled with BTX-A has a superior effect than when treated either conservatively or with BTX-A alone

In our study, group A patients were prescribed Zerodol MR, a combination of the non-steroidal anti-inflammatory drug (aceclofenac) and muscle relaxant (tizanidine). Hot fomentation and jaw exercises were recommended to the patients. One of the patients in this study had sleep bruxism, for which a night guard was provided.

Patients in group B received BTX-A injections into the trigger points of the masseter and temporalis muscles. BTX-A has progressed from a poison to a useful medical tool with an increasing variety of uses, especially in the treatment of a broad array of head and neck disorders resulting from muscular hyperfunction. When BTX-A is injected into a muscle, it causes paresis in 2–5 days, which lasts for 2–3 months before gradually diminishing. The perceived duration of action differs across individuals with the same disease and patients with different disorders. (22). We injected 10 units per trigger point in the masseter and temporalis muscles according to the manufacturer's guidelines. No allergic reactions were reported by the patients after the injections. In 2016, **Jorge Chaurand et al**. conducted a similar study on 11 patients with masseter and temporalis muscle pain. After 1 month of conservative therapy (control group) and BTX-A injections

(study group), a visual analog scale for pain and pressure algometry was performed. When compared to baseline, both conservative therapy and BTX injections produced lower pain scores and higher pain thresholds, and there were statistically significant differences between the two groups. The results in the study group were superior. (23)

BTX-A was injected into the MTrPs of the patients in group C. Patients were also instructed to take a muscle relaxant (Zerodol MR). To minimize bruising at the injection site, they were instructed to begin hot fomentation after one week. It was suggested to do jaw exercises. An occlusal splint was provided to a patient with parafunctional habit. Although improvements were noted in all groups, it was significant in group C. BTX-A was not re-injected in any of the patients. All patients were assessed 1st week, 2nd week, 6th week, and 12th week to check the efficacy of the treatment. Although conservative treatment was effective, recurrence of pain was one of the common complaints by the patients. whereas patients in group B and group C were satisfied with the treatment. The intensity of pain and episodes of headaches were greatly reduced in group C. No significant side effects of the combination were noted in group C.

Dai et al (2008) conducted a study on 30 patients With Cerebral Palsy and Spastic Equinus Foot Deformity. All patients got localized BTX- A as well as oral baclofen or tizanidine for spasticity and were examined for a total of 12 weeks. Baclofen was given to 17 children and tizanidine was given to 13. “Caregiver questionnaire” was filled out by the patients to keep track of any tizanidine or baclofen side effects, before and after the BTX-A injections. Analysis was done using the Gross Motor Functional Measurement (GMFM) and the modified Ashworth scale (MAS) for leg functional measurement and leg spasticity assessment. The tizanidine group had significantly higher mean GMFM scores than the baclofen group. The study found that using a combination of BTX-A and oral tizanidine to treat spastic cerebral palsy was more effective and had fewer side effects than using BTX-A and oral baclofen. (24)

The efficacy of the BTX-A has been thoroughly described in the literature for the treatment of temporomandibular disorders. Although it is widely considered to be safe, its widespread use raises safety concerns. The formation of antibodies to the toxin has also been documented as a long-term side effect of BTX treatment. According to pharmacovigilance data and case reports, BTX appears to be linked to serious side effects like botulism, widespread paralysis, dysphagia, respiratory depression, and even death. (25) Along with the appropriate diagnosis of the condition, the operator should be well versed with the associated anatomy of the muscles in the peri-surgical area before administering the BTX-A.

The limitation of this study is the small sample size. To our knowledge, only a few studies that combine BTX-A therapy with conservative treatment have been conducted. When patients were treated with both BTX-A injections and conservative treatment, the

results showed a significant decrease in pain as well as an increase in mouth opening, which was in line with the proposed hypothesis. A better understanding of the effect of BTX, coupled with the conservative management of MPDS, and its possible adverse effects requires multicentric RCT with a large sample size, which could provide us with more evidence to support the current study's hypothesis.

CONCLUSION:

MPDS management is primarily conservative. Rest, instructions to avoid loading, control of contributory factors like clenching or bruxism, pain relief with NSAIDs and muscle relaxants, and, in some cases, jaw exercises, splint therapy, MTrPs injections are some of the other options. While BTX-A does not promise complete pain relief, our study showed that it significantly improved symptoms, making it a valuable second-line treatment option. Botulinum toxin injections in combination with muscle relaxants have only been studied in a few studies. In our study, we discovered that there was a significant improvement in pain relief, increased mouth opening, and overall condition improvement. Our study comprised of small sample size. It is recommended to have a larger sample size to correlate with the findings.

Conflicts of Interest: none declared

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