Neuromuscular Retraining versus BTX-A Injection in Subjects with Chronic Facial Nerve Palsy, A Clinical Trial

*Abbas Ali Pourmomeny¹,(PhD); Elham Pourali¹,(MSc); Ahamd Chitsaz², (MD)

Abstract

Introduction:
Chronic facial nerve palsy has long been known to negatively affect the quality of life in patients. The present study aimed to investigate the efficacy of Botulinum Toxin A (BTX-A) and neuromuscular retraining therapy (NMRT) in the symmetry of chronic facial palsy.

Materials and Methods:
Two groups, namely experimental and control, were considered each consisting of 13 patients. The study population included a total of 15 female subjects. The BTX-A was injected into the synkinetic muscle in the experimental group; nevertheless, the patients in the second group participated in special neuromuscular retraining. The rate of reducing synkinesis and symmetrical improvement was evaluated using the Facial Grading System (FGS) after 4 months of treatment. The independent t-test was performed to compare the two groups.

Results:
According to the Sunnybrook FGS, the mean changes in Sunnybrook scores in the experimental and neuromuscular retraining groups were 3% and 24%, respectively. The comparison of the mean scores of the two groups was statistically significant after the interventions (P=0.033). A variable ratio of statistically significant improvement was observed in synkinesis in both groups following the treatment (P=0.041). In addition, by comparing the synkinesis scores between the two groups, the reduction of synkinesis was observed to be greater in the neuromuscular retraining group (P=0.041) after the treatment.

Conclusions:
The findings of the current study indicated that special neuromuscular retraining leads to significant improvement in the FGS score, compared to botulinum toxin therapy alone. Moreover, it was observed that facial symmetry can be treated with special neuromuscular retraining and the patient can overcome synkinesis.

Keywords:
Botulinum toxin A, Facial nerve palsy, Neuromuscular retraining, Synkinesis.

*Please cite this article as: Pourmomeny AA, Pourali E, Chitsaz A. Neuromuscular Retraining versus BTX-A Injection in Subjects with Chronic Facial Nerve Palsy, A Clinical Trial. Iran J Otorhinolaryngol. 2021;33(3):151-155. Doi: 10.22038/ijorl.2021.41305.2347

¹Department of Physical Therapy, School of Rehabilitation Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
²Department of Neurology, School of Medicine Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
*Corresponding Author:
Department of Physical Therapy, School of Rehabilitation Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: pourmomeny@gmail.com
Introduction

Synkinesis, muscle tension, muscle contracture, and atrophy are the most common consequences of chronic facial nerve palsy (FNP) (1). Muscle tension refers to the condition in which the muscles of the face remain semi-contracted for an extended period. Muscle contracture is a permanent shortening of a muscle or soft tissue. As an involuntary and abnormal facial movement associated with voluntary movements of other facial muscles, synkinesis is thought to be the result of misdirected sprouting, re-innervating both the original and other facial muscles (2). It has been estimated that synkinesis is diagnosed in around 15-20% of individuals depending on the case series (3,4). The appearance and progression of synkinesis may each require 3 to 4 months and up to 2 or more years, respectively (5). Accordingly, the manifestations of FNP can range from muscular contracture to tension and weakness. Furthermore, synkinesis disrupts muscular coordination and causes an asymmetrical connection between the two facial opposite sides. All four sequelae cause asymmetry in the face at rest and dynamic movements and especially the standard expression of the face is affected which significantly impacts patients’ quality of life. The application of precise and specific feedbacks during a process known as facial neuromuscular retraining can help to retain and relearn facial movements.

In addition, the aforementioned process can be beneficial in preventing unwanted muscular movements and acquiring normal facial expression, patterns, and functionality. In a previous study, BTX-A was studied as a complementary therapy for facial symmetry with biofeedback training (6).

The present study aimed to compare the effectiveness of injecting BTX-A and (NMRT) using electromyographic biofeedback (EMG-BFB) when BTX-A was infused into synkinetic muscular tissues at three to seven sites (Figure 1). The synkinesis muscles around the eye were injected with 10 to 15 units at each point, and the synkinesis muscles around the mouth were injected with 15 and 20 units. The injections were administered using an insulin syringe (7).

Materials and Methods

This clinical trial was registered in the Iranian Registry of Clinical Trials (IRCT201612136083 N10). The Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran, also approved the study protocol under the code of IR.MUI.REC.1395.3.128.

The study population was recruited by referring to physiotherapy clinics. The subjects with peripheral facial paralysis were initially examined by three specialists (including a plastic surgeon, an ear, nose, and throat specialist, and a neurologist). The inclusion criteria were having BTX-A hypersensitivity, being pregnant or in the lactating period, and suffering from either peripheral motor neuropathies or neuromuscular junction disorders, such as myasthenia gravis.

The eligible subjects were requested to give informed consent by signing a pre-prepared form. Then, the patients were randomly allocated to either the experimental (BTX-A) or control (NMRT) group. For randomization, each pair of participants was consecutively (one member in each pair was assigned to one group leading the other member to the opposite group) and randomly assigned to either group upon admission. Each patient was monitored within 8 to 12 weeks to confirm the constancy of synkinesis, and then the treatment was started. Finally, within May 1 in 2015 to May 3 in 2019, 26 patients (including 15 female and 11 male subjects) had completed treatment in the study. Table 1 shows the demographic and clinical features of the participants.

2-1. Injection

The asymmetry, synkinesis, and tension were carefully examined in the first stage. The synkinetic points were identified on the patient’s face. Then, normal saline (2.5 mL) was used to dilute BTX-A vials containing 300 units of the compound.

The diluted toxin was then infused into the synkinetic muscular tissues at three to seven sites (Figure 1). The synkinesis muscles around the eye were injected with 10 to 15 units at each point, and the synkinesis muscles around the mouth were injected with 15 and 20 units. The injections were administered using an insulin syringe (7).
**Table 1**: Demographic and clinical features

| Variable                     | BTX-A** | NMRT*** | P-value |
|------------------------------|---------|---------|---------|
| Age (mean ± standard deviation) | 43.67±10.5 years | 37.67±14.5 years |       |
| Gender                       |         |         |         |
| Male                         | 4       | 7       |         |
| Female                       | 9       | 6       |         |
| Side                         |         |         |         |
| Left                         | 11      | 7       |         |
| Right                        | 2       | 6       |         |
| Cause                        |         |         |         |
| Bell’s palsy                 | 12      | 11      |         |
| Trauma                       | 0       | 2       |         |
| Tumor (Schwannoma)           | 1       | 0       |         |
| Average number of treatments | 125     | -       |         |
| Average total cumulative dose; units (per case) | 1        | 49±3    |         |
| Average duration of disease (month) | 43.93±67 | 34.42±34 | 0.66   |
| FGS*                         | 45.14±18.2 | 39.8±16.2 | 0.97   |

* Facial Grading System; ** Botulinum toxin type A; *** Neuromuscular retraining therapy

**Fig 1**: Locations for facial injections of Dysport

**2-2. NMRT**

All the standard expressions were analyzed by a specialized physiotherapist, and the weak, contracted or tense, and synkinetic muscles were determined in each patient. In this study, a normal saline solution, as a placebo injection, was injected into the members at several points of the affected side. The NMRT included massaging the soft tissue, stretching the contracted muscles of the affected side, relaxing the tense muscles, and giving EMG-BFB for muscle strengthening and synkinesis control. After providing the patients with some preliminary data on the anatomy and various muscles of the face, along with their functions, during the 4-month treatment period, three 45-min sessions were performed each week. The participants were also taught how to control synkinesis and movement. Therefore, mirror biofeedback as home training was prescribed for each patient.

**2-3. Outcome measures**

The subjects’ facial characteristics were assessed at the baseline (before the treatment) and after the 4-month treatment period utilizing videotapes in the rest position of the face and five standard expressions. Three skilled experts who were unaware of the patients’ group assignments independently assessed the videotapes before and after the treatment. The degree of facial symmetry (in resting position, dynamic movement, and synkinesis) was evaluated by a score in the Sunnybrook Facial Grading System (FGS) (6). The SPSS software (version 16; SPSS Inc., Chicago, IL, USA) was utilized for data analysis using the two-tailed test at 0.05 as the level of significance. The patients were examined for complications, such as ptosis, at (after) a two-week post-injection.

**Results**

The baseline features of the two groups were homogeneous and showed no statistically significant difference (P=0.66; Table 1). Three patients suffered ptosis and drooling for a short time (about 10 days). The FGS composite scores and subdomains were calculated for resting symmetry, symmetry of voluntary movement, and synkinesis symmetry in both groups. In the BTX-A group, the total FGS composite scores were 45.14±18.2 and 48.36±17.5 before and after the treatment, showing an increasing but insignificant pattern (P=0.51), respectively. In comparison, the FGS composite score of the NMRT group increased from a mean of 39.83±16.2 to 64.17±10.4 (P<0.01) in the post-treatment group. The difference in the composite scores between the two groups was statistically significant after the treatment (P=0.033). The FGS subdomain synkinesis in both groups
significantly improved. The scores of subdomains of voluntary movement and resting symmetry in the BTX-A group were 66.5±15.2 to 67.14±15.3 and 11.43±3.6 to 10±3.9, respectively (Table 2), which were not statistically significant (P=0.08). The scores of subdomains of voluntary movement and resting symmetry in the NMRT group were 63±13.8 to 75±11.4 and 12.08±2.5 to 6.67±3.8, respectively, which were statistically significant.

Table 2: The results of comparing two treatment

| Group | FGS*: Pre-treatment | Mean ± standard deviation | FGS: Post-treatment | Mean ± standard deviation |
|-------|---------------------|---------------------------|---------------------|---------------------------|
|       | Rest                | Voluntary movement        | synkinesis          | FGS                        | Rest                | Voluntary movement        | synkinesis          | FGS                        |
| BTX-A | 11.43±3.6           | 66.5±15.2                 | 10±3.9              | 45.14±18.2                | 10±3.9              | 67.14±15.3                 | 7.01±2.3           | 48.36±17.5                |
| NMRT**| 12.08±2.5           | 63±13.8                   | 11.08±2.5           | 39.83±16.2                | 6.67±3.8           | 75±11.4                    | 4.17±2             | 64.17±10.4                |
| p-value| 0.23                | 0.94                      | 0.87                | 0.97                      | 0.83                | 0.035                      | 0.041              | 0.033                     |

* Facial Grading System; ** Botulinum toxin type A; *** Neuromuscular retraining therapy

**Discussion**

This has been the first study that has directly compared two treatments in patients with the sequelae of FNP. According to FGS analysis, facial nerve synkinesis was successfully managed and resolved in both groups, further confirming literature findings (6,8). Despite the decreased synkinesis scores in both groups, a lower mean score in the BTX-A group may be due to its therapeutic halftime in this group. In addition, only the FGS composite score and voluntary movement in the MNRT group increased significantly. This result is a logical consequence of active exercise, stretching, and relaxation procedures in NMRT.

The purpose of BTX-A injection is to reduce or eliminate synkinesis and indirectly modify the asymmetry in facial movement. Then, 3-10 days after using BTX-A injection, synkinesis was eliminated through the inhibition of acetylcholine release at the synapse level. Following this 4-5 month period, one of the following conditions may occur:

1) synkinesis totally vanishes;
2) synkinesis may partially relapse;
3) synkinesis may completely relapse and appear again.

It has been suggested that the infusion of BTX-A into the normal facial side may be effective in retaining symmetry (9-11). However, the asymmetry of facial palsy will not be corrected and the asymmetry may increase (12).

Given the delicacy and small size of facial muscles, they are referred to as the superficial musculoaponeurotic system (13). The voluntary and facial expression movements are performed in a pattern with minimal contraction. It is important to accurately identify the synkinesis and weak or tough muscles before treatment. It has to be noted that the analysis of facial movements is essential for the success of NMRT.

The goal of NMRT using biofeedback in FNP is enhancing the quality of movement and motor control and upgrading muscular functionality to resolve the asymmetry. Another important point is to convince patients to accept and try to treat their defect. This asymmetry either is a result of muscle weakness, increased muscular tension, or consequence of synkinesis.

The EMG-BFB facilitates neuromuscular re-education and allows providing patients with the opportunity to perceive surrounding auditory and visual signals which are naturally hidden to the patient. Through monitoring the activity of motor units during this process, the patient is also able to control the function of a muscle or a group of muscles. Using these feedback approaches, the patient is enabled to create a partial movement following taking the control of a number of motor units. Furthermore, patients can be taught how to suppress muscular motor activities (e.g., synkinesis and tension) due to a sequel of facial palsy. This phenomenon is due to the lack of proprioception producing internal sensory receptors in facial muscles (6,14).

In addition and unlike skeletal muscles, there are no facial shields for the closure of muscles in the face (6).

Contrary to some studies (15,16), the patients in the present study were in a socially active age range (mean age: 42 years). The participants had a high motivation for recovery, particularly in the NMRT group, with an average age of 37 years. The results of the current study showed
that the injection of BTX-A decreased synkinesis; nevertheless, it could not affect the weakness and contraction of the muscles. Some researchers suggest BTX-A injections more than one session for the reduction of synkinesis. However, further investigations and comparisons are necessary in this regard.

**Conclusion**

Although BTX-A injection may reduce synkinesis, it cannot affect the voluntary movement in FNP with just one session of treatment. Nonetheless, NMRT is the rational treatment for muscle weakness and synkinesis caused as the sequelae of FNP.

**Acknowledgments**

The present study was approved by the Clinical Research Council of Isfahan University of Medical Sciences and followed the related ethics guidelines. The authors would like to express their gratitude to their colleagues from Al-Zahra hospital in Isfahan and Vice-Chancellery for Research of Isfahan University of Medical Sciences for supporting this project.

**Reference**

1. Cronin GW, Steenerson RL. The effectiveness of neuromuscular facial retraining combined with electromyography in facial paralysis rehabilitation. Otolaryngol Head Neck Surg. 2003; 128: 534-8.
2. May M. Microanatomy and pathophysiology. In: May M, editor. The Facial Nerve. 2nd ed New York: Thieme; 2000. p. 57-65.
3. Bylund N, Jansson D, Enghag S, Berg T, Marsk E, Hultcrantz M, et al. Synkinesis in Bell's palsy in a randomized controlled trial. Clin Otolaryngol. 2017;42: 673-80.
4. Husseman J, Metha RP. Management of synkinesis. Facial Plast Surg 2008;:242-9.
5. Celik M, Forta H, Vural C. The development of synkinesis after facial nerve paralysis. Eur Neurol. 2000;43: 147-51
6. Pournomeny AA, Asadi S, Cheatsaz A. Management of facial synkinesis with a combination of BTX-A and biofeedback: a randomized trial. Iran J Otorhinolaryngol. 2015; 27:409-415.
7. Cabin JA, Massry GG, Azizzadeh B. Botulinum toxin in the management of facial paralysis. Current opinion in otolaryngol head neck surg.2015;23:272-80.
8. Beurskens CH G, Heymans PG. Positive Effects of Mere Therapy on Sequelae of Facial Paralysis: Stiffness, Lip Mobility, and Social and Physical Aspects of Facial Disability. Otol Neurotol. 2003; 24: 677-81.
9. Kim J. Contralateral botulinum toxin injection to improve facial asymmetry after acute facial paralysis. Otol & Neurotol. 2013; 34:319-24.
10. Sadiq SA, Khwaja S, Saeed SR. Botulinum toxin to improve lower facial symmetry in facial nerve palsy. Eye 2012;26:1431.
11. do Nascimento Remigio AF, Salles AG, de Faria J CM, Ferreira MC. Comparison of the efficacy of onabotulinumtoxinA and abobotulinumtoxinA at the 1: 3 conversion ratio for the treatment of asymmetry after long-term Plast Reconstr Surg. 2015; 135:239-49.
12. Couch SM, Chundury RV, Holds JB. Subjective and objective outcome measures in the treatment of facial nerve synkinesis with onabotulinumtoxinA (Botox). Ophthalmic Plast Reconstr Surg. 2014; 30:246-50.
13. Schaitkin B, Eisenman D. Anatomy of Facial Muscles. In: May M SB, editor. The Facial Nerve. 2nd ed. ed. New Yourk: Thieme; 2000. p. 95-105.
14. Van Swearingen Jessic. Facial Rehabilitation: A Neuromuscular Reeducation, Patient-Centered Approach. Facial Plastic Surgery 2008; 24:250-9.
15. Rogers CR, Schmidt KL, Van Swearingen JM, Cohn JF, Wachtman GS, Manders EK, et al. Automated facial image analysis: detecting improvement in abnormal facial movement after treatment with botulinum toxin A. Ann Plast Surg. 2007;58:39-47.
16. Ito H, Nakano S, Kusaka H. Low-dose subcutaneous injection of botulinum toxin type A for facial synkinesis and hyperlacrimation. Acta neurologica scandinavica. 2007; 115:271-4.