Botulinum Toxin in the Treatment of Facial Synkinesis and Hyperkinesis

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Objectives/Hypothesis: Facial synkinesis and hyperkinesis commonly impair the outcome of facial nerve palsy. Botulinum toxin type A has shown positive results in the treatment of these symptoms. Our experience is reported in this article.

Study Design: Prospective study.

Methods: Forty-one patients affected by facial synkinesis and hyperkinesis due to facial palsy were treated. The etiology of the facial palsy was: 28 Bell’s palsy cases, nine iatrogenic cases (seven acoustic neuroma surgeries, one tympano-jugular glomus tumor removal, and one middle ear surgery), three herpes zoster virus cases, and one case of Melkerson-Rosenthal syndrome. Botulinum toxin type A was used in the treatment. Clinical evaluation was obtained through the Sunnybrook Grading Scale and an author’s modification of this method purposely designed for evaluation of hyperkinesis. Further evaluation through a self-administered synkinesis questionnaire was also performed.

Results: All patients showed some improvement of synkinesis and hyperkinesis after treatment. The mean values of the data obtained, regardless of the method of evaluation, gave statistically significant results. Correlation between objective and subjective evaluation methods was also statistically positive.

Conclusions: This work stresses the importance of considering synkinesis and hyperkinesis separately because they are different conditions. These two symptoms showed improvement after botulinum toxin treatment, but only hyperkinesis showed a positive correlation when objective and subjective evaluations were performed. This treatment is effective in the management of facial synkinesis and hyperkinesis due to facial palsy, thus improving quality of life. It is a safe, minimally invasive treatment that can be repeated.

Key Words: Synkinesis, hyperkinesis, botulinum toxin, facial palsy.

Level of Evidence: 1b.

INTRODUCTION

Facial palsy, regardless of its etiology (i.e., infective, iatrogenic, or traumatic) in the healing process often produces involuntary static and dynamic alteration of facial expression. This is due to aberrant regeneration of fibers in the neural repair process. Such irregular and massive regeneration may lead to several unwanted effects, including synkinesis, which is characterized by synchronous and involuntary movements of certain areas of mimic muscles. This becomes particularly visible when spontaneous facial movements occur, especially during emotional expressions such as involuntary blinking or smiling.1,2 Hyperkinesis is another undesired secondary effect of facial palsy recovery, which consists of static and dynamic asymmetry of the face due to hypertonia. Hyperkinesis is typically responsible for a narrow eye, a more pronounced nasolabial fold, and the corner of the mouth pulled laterally up or down. These alterations can lead to many psychological and social problems, including physiognomic alteration and communication problems, which often cause embarrassment and lack of overall well-being, self-esteem, social acceptance, and poor quality of life. Numerous facial rehabilitation techniques after facial palsy have been developed to improve cosmesis and function, including minor operations such as medial canthoplasty, eyelid weight, brow lifts, orbicularis myectomy, or major surgery such as facial-hypoglossal anastomosis, vascular free muscle grafts, and cross-facial surgery.3 Initially, these methods were developed to treat facial palsy and not to ameliorate synkinesis or hyperkinesis. For many years, botulinum toxin (BT) chemical neurectomy was considered a good approach in treating these conditions.2,4,5 BT is a protein derived from a bacterium (Clostridium botulinum), and is present in seven serologic types, including A, B, C, D, E, F, and G.6–8 Botulinum toxin type A (BT-A) is the most powerful and common form used for treatment in humans. The action mechanism is the blocking of the presynaptic release of acetylcholine, which causes a temporary functional denervation of neuromuscular end plates. Collateral sprouting reestablishes the pathological state after a period of 3 to 6 months.6,7 BT was first used by Scott et al. in strabismus patients,9 and the U.S. Food and Drug Administration (FDA) approved BT for the treatment of...
strabismus in 1979. Further pathologies approved by the
FDA were hemifacial spasm and blepharospasm (1989),
although it had already been used for blepharospasm
treatment since 1982. The goal of the present study
was to demonstrate the efficacy of BT therapy in the
 treatment of synkinesis and hyperkinesis after facial
palsy.

MATERIALS AND METHODS
From September 2008 to December 2010, a total of 41
patients affected by synkinesis and hyperkinesis consequent
to facial palsy were treated with BT. The etiology of the facial
palsy was 28 Bell’s palsy cases, nine iatrogenic cases (seven
acoustic neuroma surgeries, one case of tympano-jugular glo-
mus tumor removal, one case of middle ear surgery), three
herpes zoster virus cases, and one case of Melkersson-Rosenthal
syndrome. The affected sides were 23 left and 18 right; the
mean age was 47 years (range, 16–80 years); The gender break-
down was 28 female and 13 male patients. Written consent was
obtained prior to treatment.

Procedure
Pre- and post-treatment pictures and short video clips of
patients were taken with a Nikon camera (Coolpix 12.1 MP, VR,
ISO 3200; Nikon, Tokyo, Japan) at 1 m distance and a focal
length of 26.3 mm.

We administered BT-A (Botose; Allergan Pharmaceuticals
Ireland, Westport, Ireland). We diluted 100 U of BT-A in 2.5 mL
of 0.9% saline (concentration 4 U/0.1 mL), and injections were
administered subcutaneously after application of lidocaine/prilo-
caine cream (EMLA; AstraZeneca, Milan, Italy), with an
insulin-type syringe and 30-gauge needle. For superior facial
area injections (orbicularis oculi, corrugators, and frontalis
muscles), the syringe was equipped with a 4-mm needle (Mesol-
relle; Gallini S.P.A., Mantova, Italy). For middle and inferior
areas (zygomaticus, levator muscle of upper lip, orbicularis oris,
depressor labii, depressor oris, and platysma muscles) and con-
sidering muscle depth and thickness, a 12.7-mm needle (BD
Microlance, Drogheda, Ireland) was used. Patients with histor-
ies of hypersensitivity to any BT-A constituent or showing
pregnancy, lactation, neuromuscular junction disorders (mysste-
nia gravis), peripheral motor neuropathies, or active infections
were excluded.

The injection points and doses were: eyebrow corrugator
muscle, 2 to 4 U; orbicularis oculi muscle, 5 to 8 U; zygomaticus
muscle, 2 to 4 U; corner of the mouth, 2 to 4 U; depressor mus-
icle anguli oris, 1 to 2 U; mentalis muscle, 1 to 2 U; levator labii
superioris, 1 to 6 U; and platysma muscle, 3 to 6 U. The injec-
tion angle was always 45°.

Clinical Evaluation
Clinical evaluation was obtained through Sunnybrook
Grading Scale (SG) and self-administration of the Synkinesis
Assessment Questionnaire (SASAQ). The SG facial grading
system is based on the evaluation of resting symmetry, degree
of voluntary excursion of facial muscles, and degree of synkine-
sis associated with specified voluntary movement. This scale
indicates the facial impairment level, ranging from 0 (complete
palsy) to 100 (complete recovery), and allows a separate analy-
sis of synkinesis by assessing the different regions of the face
and the severity, through a grading system based on a score
between 0 and 15. In our study, we divided patients into four
subgroups: 0 = none, 1 to 5 = mild, 6 to 10 = moderate, and 11
to 15 = severe. For more complete results, synkinesis and
hyperkinesis were evaluated separately. To accomplish this,
hyperkinesis grading was performed using a modified SG. Table
I shows the modified SG for hyperkinesis evaluation. Severity
is indicated by the score obtained by summing facial deformity
scores, 0 points meaning normality (symmetrical face at rest), 1
to 3 points indicating mild-moderate hyperkinesis, and 4 to 6
points representing high severity. For the SASAQ, patients
were invited to answer nine questions. The scores ranged from
9 to 45 points (with 9 meaning normal, and 45 indicating
extremely severe synkinesis). Both treatment and subsequent
result evaluation were performed by three different otolaryngol-
ogists. Patients were evaluated after 10 days and after 1
month.

RESULTS
A total of 325 injections were performed in the vari-
ous facial districts (the mean value of number of
injections for each patient was 7.9). BT-A adverse reac-
tions were rare and mild. They included eye dryness

![Graph](https://via.placeholder.com/150)

Fig. 1. Patient distribution before and after treatment according to the Sunnybrook Grading Scale. Bt SB = Sunnybrook Scale before treatment; At SB = Sunnybrook Scale after treatment.
(three cases), mild zygomatic hematoma (three cases) that lasted a maximum of 6 days, mild lagophthalmos (one case), and ptosis in one patient affected by Horner syndrome that lasted for 8 weeks. No one showed diplopia. For treatment efficacy results, we analyzed improvement separately according to the three different evaluation methods. Figure 1 shows patient distribution before and after treatment according to the SG. The pretreatment mean value was 56.0, whereas the post-treatment value was 70.3. A high degree of significative-ness was confirmed in all patients using t tests \( (P < .001) \). Figure 2 shows pre- and post-treatment patient distribution according to the synkinesis grade of severity.

The pretreatment mean value (absolute) was 8.05, whereas the post-treatment value was 3.4. The analysis of the four groups shows an apparent increase in the none and mild groups, which is due to the shift of patients coming from the moderate-severe groups that disappeared completely. Figure 3 shows the hyperkinesis evaluation results obtained through the modified SG. All of the patients reported an improvement of this symptom. Despite the disappearance of the severe group, a significant number of patients showed some hypertonia. Pretreatment (absolute) mean value was 2.7, whereas the post-treatment value was 0.7 (score range, 0–6; 0 = normal and 6 = severe hyperkinesis). Figure 4 shows patient distribution and related value of the SASAQ evaluation method before and after treatment. The pretreatment mean value was 28.2, whereas the post-treatment value was 15.8 (score range, 9–45; 9 = normal and 45 = severe synkinesis-hyperkinesis). This subjective method is extremely reliable and was confirmed by statistical analysis \( (P < .001) \). Table II summarizes the correlation between subjective (SASAQ) and objective methods (hyperkinesis and synkinesis). Values show significant correlation between SASAQ and hyperkinesis \( (P < .05) \), whereas the correlation between SASAQ and synkinesis was not significant. Correlation is significant when it reaches a .05 level.

**DISCUSSION**

This study demonstrated the efficacy of BT-A in the treatment of both postparetic synkinesis and hyperkinesis, thus confirming literature findings. Most of the studies available focus on synkinesis. Sunderland described five possible degrees of peripheral nerve fiber injury and six groups of spontaneous recovery 1 year after injury. Inter-mediate situations (groups II–V) showed faulty regeneration consisting of crocodile tears, stapes tendon contraction, hemifacial spasm, facial myokymia, blepharospasm, and habitual tic, in addition to synkinesis and hyperkinesis, which were the most frequently observed sequelae. Synkinesis is an abnormal synchronization of movement, occurring with voluntary and reflex activity of muscles that normally do not contract together. Hyperkinesis is an excessive contraction of a muscle group and usually occurs together with a hyperexcitability of muscle response to electrical nerve stimulation. This results in an unaesthetic facial look both at rest and during movement. The eyes usually look smaller, and this conflicts with previous palsy lagophthalmos, which makes the eyes look bigger. The commissure of the mouth looks lateralized, thus making the healthy side look palsied. Moreover, the nasolabial folds seem deeper, and this conflicts with their flattening during previous palsy.

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**Fig. 2.** Pre- and post-treatment patient distribution according to the synkinesis grade of severity.

**Fig. 3.** Results in terms of hyperkinesis evaluation obtained by means of the modified Sunnybrook Grading Scale.
In this study we analyzed these two pathological movements (i.e., hyperkinesis and synkinesis) separately, and this led us to partially modify the SG to separate the two phenomena, which in the aforementioned scale are together, and analyze them individually. Comparison of the results obtained through subjective data assessment (SASAQ self-evaluation) with the data collected through objective observation methods (synkinesis and hyperkinesis) only shows a positive correlation between SASAQ and hyperkinesis, but no correlation at all between SASAQ and synkinesis. This can probably be explained because patients are happier when looking at themselves in the mirror and seeing a symmetry improvement at rest and during movements (hyperkinesis), whereas they do not appreciate sufficiently the objective improvement of synkinesis, especially during the blink reflex. This analysis was possible after modifying the SB grading scale. We think that the above-mentioned scale shows some limitations in that it analyzes the two disorders together.

Our study also stresses the importance of establishing a precise infiltration method regarding both infiltration areas/points and depth. In our view, different thicknesses of muscular-skin units can lead to different treatment efficacy and adverse reactions. For better results, we deem it very important to vary the needle length for injections in the upper areas of the face (thin skin) on the one hand and median-lower areas (thicker skin) on the other hand. The 45°-needle angle is also important to prevent some side effects, including diplopia and ptosis, due to infiltration in the eye’s extrinsic muscles and in the eyelid’s levator muscle. Doses and points of injection varied individually and depended on the severity of synkinesis or hyperkinesis, as well as the muscles involved. We followed some complication prevention guidelines, including four injections around the orbicularis oculi and injection of the upper part of this muscle, which should not be too peripheral in the upper lid to avoid ptosis of the levator palpebrae muscle. Injection in the lower lid should not be too medial, as it could cause epiphora (paralytic ectropion resulting as a side effect). We invited our patients to look straight ahead to determine and exclude the upper and lower lids’ portions corresponding to the iris area and infiltrate out of this area 5 mm from superior and inferior lid edges. Injections were performed at a 1- to 1.5-cm distance from the mouth corners. In our experience, side effects were less serious and less frequent using smaller overall toxin doses administered in smaller aliquots, not to compromise the response. As a protocol for initial treatment, we would recommend 5 to 8 U in total at four injection sites around the eye. As far as the middle and inferior districts are concerned, a total of 2 to 6 U were administered at three injection sites around the mouth. Although the eye injection site accuracy is of paramount importance, the most serious injection complication in the lower third of the face due to overdosing is respiratory insufficiency caused by vocal cord paralysis. The data reported in this study were collected 30 days after injection. Denervation process starts a few hours after injection, but becomes clinically visible after 2 to 10 days. Nerve-ending sprouting and synaptic contact development allow junction recovery over 2 to 3 months. Therapeutic effects vary depending on the pathology, the severity of the pathological movement, the doses injected, and patient responsiveness. Once a patient’s responsiveness to the toxin is known, the same dose may be administered again or adjusted accordingly.

CONCLUSION

This study demonstrated the efficacy of BT-A in the treatment of both postparetic synkinesis and hyperkinesis. The data reported are statistically significant. For accurate result evaluation, the authors deemed it necessary to develop two specific scales, one for synkinesis and one for hyperkinesis. Botulinum therapy was demonstrated to be a safe procedure and its side effects mild and transient, usually lasting only a few weeks until recovery. Injection accuracy (in terms of depths and sites) is key to quality results.

BIBLIOGRAPHY


