

## Editorial

# The Role of Botulinum Toxin Injections in the Treatment of Facial Nerve Palsy

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Received: October 01, 2014; Accepted: November 16, 2014; Published: November 19, 2014

## Introduction

The treatment of facial nerve palsy is complex and often requires multiple interventions to restore function and symmetry to the face. Botulinum toxin injections treat complications of facial nerve palsy such as synkinesis, facial asymmetry and contralateral hyperkinesis. The use of botulinum toxin to treat facial asymmetry began in the 1980s and expanded to treat synkinesis in the early 1990s. Since this time many studies have shown its effectiveness to improve facial symmetry as well as function of the paralyzed face [1-8].

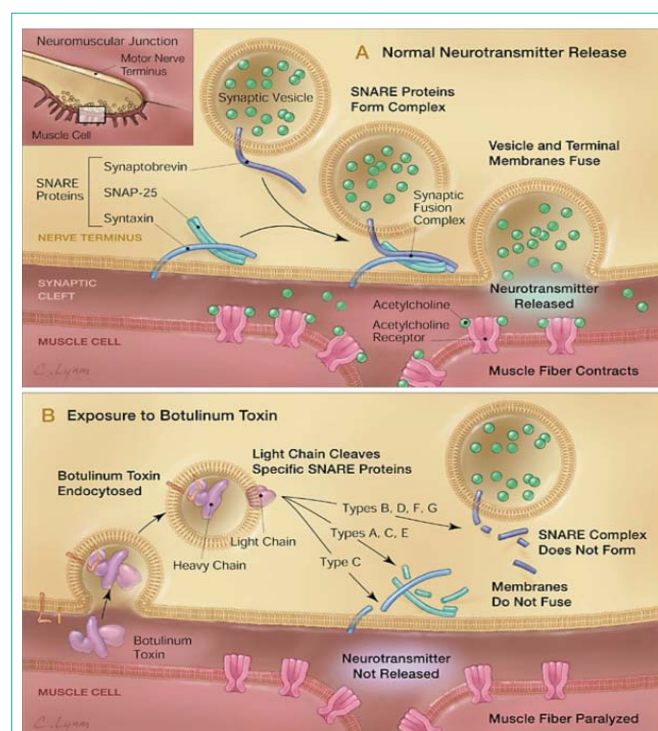
Botulinum toxin type A produces chemodenervation of the injected muscle by inhibiting presynaptic acetylcholine release from nerve terminals. Specifically, once the toxin is internalized by endocytosis into the nerve axon, inhibition of SNAP-25 (synaptosomal associated protein-25) on the cell membrane blocks acetylcholine release, in turn preventing muscle contraction (Figure 1). The onset takes 2-3 days with maximum effect occurring at 2 weeks. Binding of the toxin to the nerve is irreversible, and recovery of muscle function is due to collateral axonal growth to restore the motor synapse. The chemodenervation effect of botulinum toxin reverses in 3-5 months, depending on site of injection, often requiring repeat injections to maintain results [9]. Two commercial formulations of botulinum toxin type A are available: Dysport and Botox, generically known as AbobotulinumtoxinA (ABO) and OnabotulinumtoxinA (ONA), respectively. Comparison of these two preparations in frontalis injections have shown earlier onset and longer duration of improvement using ABO (Dysport) compared to ONA (Botox). However, the two preparations have similar effectiveness. A dose ratio of ONA to ABO for frontalis injections of 2.5:1 has been effectively used [10-11].

The use of botulinum toxin in the treatment of facial nerve paralysis can be divided into achieving symmetry by contralateral (or non-paralyzed) chemodenervation as well as the treatment of ipsilateral (or paralyzed) synkinesis.

## Achieving Symmetry

Management of the paralyzed face can be divided into the upper third, middle third, and lower third/neck as described previously

by Byrne et al [12] (Figure 2). The upper third of the face can further be divided into the management of the forehead and orbit. Treatment of contralateral forehead rhytids on the non-paralyzed side is a quick, easy, and effective method to achieve symmetry. Care must be taken to prevent significant contralateral brow ptosis; however a small degree may be tolerable given the likely ipsilateral brow ptosis. Conservative management of the orbit can further be divided into the brow position and the eyelids. OnabotulinumtoxinA has a limited role in the treatment of the contralateral brow as this can lead to significant contralateral brow ptosis with visual field impairment. Small amounts used in the upper to middle half of the frontalis can achieve some brow descent. Surgical brow lift via the



**Figure 1:** A, Release of acetylcholine at the neuromuscular junction is mediated by the assembly of a synaptic fusion complex that allows the membrane of the synaptic vesicle containing acetylcholine to fuse with the neuronal cell membrane. The synaptic fusion complex is a set of SNARE proteins, which include synaptobrevin, SNAP-25, and syntaxin. After membrane fusion, acetylcholine is released into the synaptic cleft and then bound by receptors on the muscle cell. B, Botulinum toxin binds to the neuronal cell membrane at the nerve terminus and enters the neuron by endocytosis. The light chain of botulinum toxin cleaves specific sites on the SNARE proteins, preventing complete assembly of the synaptic fusion complex and thereby blocking acetylcholine release. Botulinum toxin types B, D, F, and G cleave synaptobrevin; types A, C, and E cleave SNAP-25; and type C cleaves syntaxin. Without acetylcholine release, the muscle is unable to contract. SNARE indicates soluble NSF-attachment protein receptor; NSF, N-ethylmaleimide-sensitive fusion protein; and SNAP-25, synaptosomal-associated protein of 25 kd.

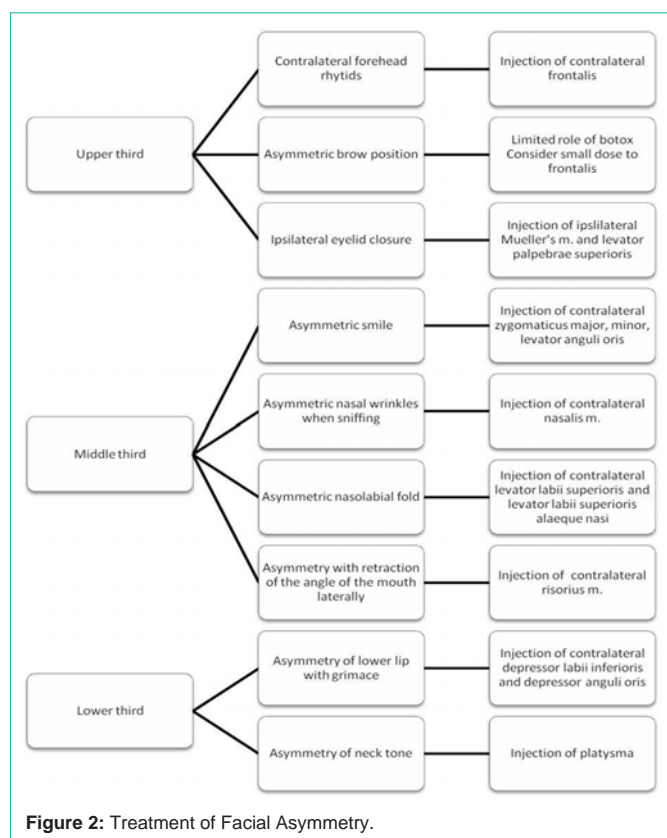


Figure 2: Treatment of Facial Asymmetry.

various described approaches is the preferred method of treatment. The primary management of lagophthalmos to prevent exposure keratopathy remains conservative measures such as lubricating eye drops and ointment as well as moisture chambers [13]. However, OnabotulinumtoxinA has been described in the use of non-permanent facial paralysis with treatment to Mueller's muscle and the levator palpebrae superioris as a temporary measure to protect the cornea [14]. This induced "iatrogenic ptosis" has been shown to provide temporary protection of the cornea during a recovery period, and can sometimes preclude the need for more invasive procedures [14]. The senior author has had minimal experience with this method as oftentimes patients with acute palsy do well with conservative measures. Ophthalmologic consultation should be obtained in all patients presenting with lagophthalmous.

Conservative management of the asymmetric middle third of the face largely targets the asymmetric smile in the upper lateral direction via chemodenervation of the anguli oris elevators (zygomaticus major and minor and the levator anguli oris) [5]. Other midface muscles described in the literature include the nasalis muscle (asymmetry of nasal wrinkles when sniffing), the levator labii superioris and levator labii superioris alaeque-nasi (asymmetry of the medial third of the nasolabial fold when sniffing), and the risorius (asymmetry at retraction of the angle of the mouth laterally) [5]. This author has significant experience with respect to chemodenervation of the zygomatic major and minor; however the patient must be extensively counseled on the risks of causing a significantly weakened smile. It is advisable to start with small doses (2-2.5 units of OnabotulinumtoxinA) and performs the injection under EMG guidance.

The lower third of the face and neck includes management of

the lower lip depressors (depressor labii inferioris and depressor angulioris) as well as the platysma muscle. This asymmetry manifests in the lower lip, and becomes more apparent when patients show their lower teeth [5]. This author has had excellent results with platysmal injection, but oftentimes requires slightly higher doses. Typical starting doses for onabotulinum toxin A in the platysma range from 15- 30 units per side. Reported complications of contralateral injections to treat the lower third of the face include mild impairment of speech, eating and drinking, however none required additional treatment or lasted beyond 28 days post-injection [5].

Contralateral hyperkinesis occurs as the non-paralyzed side of the face acts chronically against the weakened contralateral muscles. It presents with muscular hypertrophy and over activation. Abnormal facial expressions can worsen with time [15]. As with facial asymmetry due to normal kinetic movement of the non-paralyzed face against the paralyzed side as described above, hyperkinesis can occur in the forehead, ocular, midface and oral region with similar treatment strategies. Long-term benefits have been seen after the injection of OnabotulinumtoxinA into contralateral hyperkinetic muscles. At 1 month, EMG and facial disability index showed significant improvement in facial symmetry in both resting and dynamic states. This change was due to the decreased movement of the injected contralateral facial muscles, as well as an 18% increase in motion of the paralyzed side of the face. At 6 months, the injected contralateral muscles no longer showed decreased movement, however, overall symmetry was still improved due to the continued increased function of the paralyzed face [5]. Increased movement of the paralyzed face after contralateral ONA injections has been repeated in other studies as well [6,7].

## Synkinesis

Synkinesis is the involuntary motion of one area of the face occurring during the intentional movement of another area of the face. Its mechanism is thought to be multifactorial, primarily due to aberrant nerve regeneration after injury to non-intended muscle groups, but may also be caused by stimulation of neighboring axons at the site of injury due to loss of myelin and central hyperexcitability of the facial nucleus. It is named by combining the intended motor group followed by the unintended motor group. Treatment consists of OnabotulinumtoxinA injection into the synkinetic unintended motor group [16]. Common combinations of synkinesis include oral-ocular, ocular-oral, ocular-glabellar, platysmal and mentalis synkinesis. In oral-ocular synkinesis, patients intending to smile pucker or grimace will involuntarily close their eyelid. Ocular-oral synkinesis occurs when voluntary eyelid closure results in involuntary oral movement. Both of these actions also serve to deepen the nasolabial fold, further adding to facial asymmetry as described above. Platysmal synkinesis results in involuntary contraction of the lower face and neck with facial expression. This action may lead to long-term downturning of the oral commissure. Mentalis synkinesis results in puckering of the chin with facial movement [8,15].

Several studies have shown the effectiveness of OnabotulinumtoxinA for this indication. For example, in the treatment of oral-ocular synkinesis, in a double-blinded, randomized control study, 36 patients underwent injection of the orbicularis oculi with either ONA or saline. Synkinesis was evaluated by assessing for

palpebral closure with smiling, puckering and chewing; subjects in the ONA groups expressed a significant reduction in their synkinetic score compared to controls [17]. A second study showed that synkinesis disappeared in 7 of 11 patients after 3 or fewer sessions of ONA injections, suggesting that the benefit of ONA can outlast the duration of the chemodenervation it causes for permanent reduction of synkinesis [18].

Reported complications of OnabotulinumtoxinA injections for synkinesis include ptosis, keratitis, lagophthalmos, tearing and lip drop [6]. As most of these complications result from over-injection of the orbicularis oculi, a study was conducted to test the efficacy of low dose ONA (0.5-1.25U per injection site) to the orbicularis oculi. Significant improvement in synkinesis was observed in subjects with this lower dose. Therefore, a reasonable method to treat synkinesis is to begin with a low dose injection, followed by increased dosage titrations to achieve chemodenervation of intended muscle groups while limiting side effects [18].

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