Cosmetic Uses of Botulinum Toxins for Lower Aspects of the Face and Neck

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PAUL YAMAUCHI, MD

Abstract. The ability of botulinum toxin A (BTX-A) to improve the appearance of facial lines was first reported among patients who had been receiving injections for facial dystonias or surgical procedures. Since that time, there has been very extensive use of this treatment for relaxation of a wide variety of facial muscles and also for platysmal lines of the neck. Considerable experience over the last decade or longer confirms the safety and efficacy of BTX-A in the treatment of upper facial lines. BTX-A has been used also lower facial indications, but published papers are mainly uncontrolled observations on patients. Unlike the placebo-controlled studies on the upper face, there is a lack of controlled studies for lower face and neck BTX-A treatment. This article will summarize the use of BTX-A for the lower face and its role as combination treatment. Examples of combinations that may be used with BTX-A resurfacing, nonablative skin rejuvenation and skin fillers. Although little used at present, Botulinum Toxin B will be briefly discussed.

Botulism causing muscular palsy as a result of food infected with Clostridium botulinum was identified in 1897. Alan Scott, an ophthalmologic surgeon in San Francisco, developed the concept of using local injections of BTX-A to selectively inactivate ocular muscles that result in strabismus, while looking for a nonsurgical approach to correcting this condition. Subsequently, a wide variety of medical uses for BTX-A have been found, for example, treatment of dystonias, strabismus, blepharospasm, muscle spasticity disorders and torticollis, as well as spasticity in Parkinson’s disease. More recently, BTX-A has been shown to be highly effective as a treatment for hyperactive facial lines of the upper face, forehead, periorbital, nasolabial, perioral, lower facial, and nasolabial regions. In addition, the use of this agent to improve certain features of neck aging has been proven in clinical observations.

The use of a variety of minimally invasive techniques, eg, laser skin resurfacing, nonablative laser rejuvenation, and the use of dermal skin fillers, have all been shown to be highly effective in improving the aging face while reducing the need for more invasive surgery. Use of BTX-A before these procedures and while the improvement effects of these treatments are expected to occur, (over the first 12 months following laser resurfacing and nonablative laser rejuvenation,) helps to maintain a less mobile dermis, which is felt to produce a more uniform improvement of the areas treated (Table 1).

In addition, the adjunctive use of BTX-A to deep glabellar folds, lips, and perioral rhytides in combination with dermal fillers also appears to extend the life of temporary fillers.

Types of BTX-A

Botox®

There are two principal types of BTX-A currently available. Most esthetic studies reported to date relate to the use of Botox® (Allergan Inc, Irvine CA). To produce this toxin, cultures of C. botulinum are fermented and the culture undergoes autolysis, releasing BTX complexes that are then harvested by centrifugation and acidification. The quality of active toxin Botox® is defined as 1U, being the lethal dose of toxin causing death in 50% (LD50) of a group of Swiss Webster female mice. It is interesting to note that the mouse assay, which is still the standard of measuring potency of commercially available toxin, is a relatively crude assay. The original assay utilized by the Scott et al was that of LD50 in the monkey, in whom the lethal dose range is apparently less narrow than that in mice.

Lethal doses in humans are not known precisely for the purified toxin but have been estimated from a variety of published clinical catastrophes. The dose of ingested toxin would need to be 10,000–1 million times the parenteral dose. It has been estimated that an adult male weighing c. 100 kg would succumb to a dose of toxin 3500 times that needed to cause paralysis and
death in mice, ie, 3500 U of Botox.® Other data from Scott’s studies suggest that a 70-kg human would require a dose of 2800 U for an LD50 dose. In other words, there is a wide safety margin on the amount of Botox® used for therapeutic purposes, eg, for facial expression lines, a maximum of 60 U per treatment session is typical.

The procedure of purification of the human serum albumin is felt to be such that it will not allow transfer of communicable diseases.

One vial of Botox® contains 100 mouse LD50 units.

Botox is approved in several countries including the United States, Canada, France, and Switzerland for treating glabellar frown lines and in the United Kingdom for axillary hyperhydrosis.

**Dysport™**

The “European” BTX-A is called Dysport™. It was originally produced by Porton Products in the UK and was licensed for distribution via the Department of Health and Social Security by Speywood. The preparation has been used successfully for blepharospasm and torticollis.

It is difficult to accurately predict the comparative potency between Botox® and Dysport™. It is now distributed by Ipsen in France. It is not currently approved for either esthetic use or hyperhydrosis although studies are being conducted in the United States, Canada, and France.

There are no published esthetic guidelines or standards for converting between the two products. Dysport™ is available in 500 Dysport U per vial. The author has extensive experience of the use of Botox® in the United States and of both Botox® and Dysport™ in the UK. Table 2 lists some of the features of the two commercial preparations.

Dysport may diffuse more than Botox (NJ Lowe unpublished observations) which may make it a less precise BTX-A, this is why NJ Lowe prefers Botox in each such as crows feet or lower face.

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**Table 1. Some combination treatment options with Botulinum Toxin for the lower face**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Potential combination treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lip rhytides</td>
<td>Photoprotection</td>
</tr>
<tr>
<td>Marionette “sad” lines</td>
<td>Topical therapy</td>
</tr>
<tr>
<td>Prominent nasolabial folds</td>
<td>Glycolic acid peels</td>
</tr>
<tr>
<td>Facial asymmetric e.g. III nervepalsy</td>
<td>Laser skin resurfacing</td>
</tr>
<tr>
<td>“Poppy Chin”</td>
<td>Nonablative laser or intense pulse light rejuvenation</td>
</tr>
<tr>
<td>Perioral</td>
<td></td>
</tr>
<tr>
<td>Lower face</td>
<td>Chemical peels</td>
</tr>
<tr>
<td>Neck lines</td>
<td>Dermal fillers</td>
</tr>
</tbody>
</table>

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**Table 2. Details of Botox and Dysport™**

<table>
<thead>
<tr>
<th></th>
<th>Botox®</th>
<th>Dysport™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Allergan USA Irvine, CA</td>
<td>Ipsen Ltd France (manufactured UK)</td>
</tr>
<tr>
<td></td>
<td>Allergan UK High Wycombe</td>
<td>Buckinghamshire, UK (manufactured Ireland)</td>
</tr>
<tr>
<td></td>
<td>Allergan UK High Wycombe</td>
<td>Buckinghamshire, UK (manufactured Ireland)</td>
</tr>
<tr>
<td>Availability</td>
<td>100 U per vial</td>
<td>500 U per vial</td>
</tr>
<tr>
<td>Recommended storage before reconstitution</td>
<td>−5°C</td>
<td>Room temperature</td>
</tr>
<tr>
<td>Suggested diluant</td>
<td>Nonpreserved saline but often used with preserved saline</td>
<td>Nonpreserved saline but may be used with preserved saline</td>
</tr>
</tbody>
</table>

Nonpreserved saline seems to offer no reduction in Botox® potency but reduces the pain of injection (12).

**Comparison of the Potency of Botox® and Dysport™**

**Dilution Guidelines**

The author feels that 1 U of Botox® has an approximate potency of 5 U of Dysport™. Based on these potency estimates and the units per vial of Botox® (100 U) and Dysport™ (500 U), the conversion factor should be approximately a dilution 2.5 mL of saline for Botox giving a dilution of 4 U per 0.1 mL. A dilution of 2.5 mL of per Dysport™ gives an approximately equivalent potency of 20 U per 0.1 mL.

Using a 1 (Botox) to 5 (Dysport) conversion gives the following doses: Botox, 100 U per vial diluted by 2.5 mL = 4 U per 0.1 mL; Dysport, 500 U per vial diluted with 2.5 mL of saline = 20 U per 0.1 mL.

**Average Units Used for Treatment of Face**

**Upper Face**

For the upper face, average units used is as follows: 0.2 mL Botox (8 U) per corrugator muscle; 0.2 mL Dysport (40 U) per corrugator; 0.1 mL (4 U Botox, 20 U Dysport) to the procerus muscle; 0.1 to 0.15 mL to 0.3 mL (12 U Botox, 60 U Dysport) to each crow’s-feet area.

**Lower Face**

For the lower face, average units used is as follows: depressor angular oris, 2 to 4 U Botox and 10 to 20 U Dysport; mentalis, 4 to 6 U Botox and 20 to 30 U Dysport.

**Neck**

Each site into platysma spaced about 4 cm apart inject with 4 U Botox or 20 U Dysport.

**Botulinum Toxin Type B (BTX-B)**

In January 2001, BTX-B was approved for cervical dystonia. This toxin was developed by Elan Pharmacuti-
cals; its name in the USA is Myobloc® and in Europe, NeuroBloc®. Pilot studies comparing BTX-A with BTX-B have been reported.6,11 One theoretical conversion of relative potency is 1 U of Botox® to 50 U of Myobloc® based on activity in cervical dystonia. This did not give as long a duration of affect for glabellar lines as Botox®.6

BTX-B may be used with patients who develop resistance to BTX-A. However, this problem is very rare; in fact, with the latest Botox® formulations, which contain minimal quantities of protein, there have been no reports of the formation blocking antibodies (R Aoki, personal communication, 2002). Dose ranging studies with BTX-B have been published.13 It does reduce facial lines, but recent studies suggest faster onset but shorter effect than with Botox.14 There are no publications comparing Dysport with BTX-B.

Lower Facial Areas

General Comments

In general, the lower face has to be approached with more cautious doses and accurate delivery of BTX-A than the upper face. There are no published dose finding controlled studies for BTX-A on the lower face, although I and others stress that lower doses of BTX-A are used for the lower face muscles.9,10,15 Some also recommend the use of a monopolar EMG machine in areas such as the platysmal bands and some lower facial muscles.9,10

It is my practice to use a monopolar EMG machine (Accuguide, Medtronics/Xomed) for injecting the zygomatic muscles (to reduce deep nasolabial folds) in some patients with marionette lines due to overactive gomatic muscles (to reduce deep nasolabial folds) in some patients with marionette lines due to overactive

The response of the lower facial muscles to BTX-A is greater than that of the upper facial muscle for an equivalent BTX-A dose. Therefore the doses for the lower face needs to be lower by at least one half to one third per muscle compared to the upper face, eg, each corrugator muscle will be injected with between 8 to 20 U of Botox depending on the bulk and strength of the muscle, but for the lower face eg, depressor anguli oris the maximum dose is usually 2 to 4 U to each side when trying to reduce melomental folds.10,15

For zygomatic muscle injections to lessen the depth of nasolabial folds the usual dose is 2 U maximum to each side.10

Another observation is that BTX-A injection into some lower facial muscles will have a longer lasting effect eg, up to 6 months or longer compared to the effects of BTX-A on corrugator or obicularis oculi of about 4 to 5 months.10

Unwanted effects on lower facial muscles also last longer and can be cosmetically and functionally distressing.16

Possible Lower Facial Areas for Botulinum Toxin Treatment

Nasolabial Folds

These folds extend from the ala nasi to the lateral aspect of the lips. They can become deep, aging, or unattractive as a result of loss of subcutaneous tissue with age or lipoatrophy. In most patients, a variety of fillers or implants are the optimum treatment. However, some patients can benefit from injection of small (1 U Botox) to each lip elevator group of muscles—levator labii superiors alaeque nasi or zygomaticus major and minor. The position of the BTX-A injections has to be determined by examination of the facial movements of the patients often assisted by EMG-guided injections.

Too high a dose can lead to flattening of the lip and also lower facial asymmetry if injections are not placed into symmetrical positions. These problems can last for several weeks or months.10,15,16

Perioral Lines

Again, there are a number of causes of perioral lines, including photoaging, smoking, loss of subcutaneous tissue from the lower face, and reflective action of obicularis oris muscles. The use of BTX-A is usually reserved for patients with deep perioral lines worsened by lip “pursing.”

A maximum dose of 2 U of Botox is injected into each half of the upper lip. The total dose and position of injection is usually varied by patient examination before and during perioral muscle injection.5,10,15 The dose may be slightly lower ie, 1 to 1 ½ units per side into lower lip rhytides.

Prospective patients must be warned about possible effects on their ability to use their perioral oral muscles to control speech (eg, to pronounce “hard” letters such at P. Patients who sing or play musical instruments are not good candidates for perioral BTX-A.

Patients who have, and wish to retain a cupid bow of the upper lip should not be injected in the middle upper lip.

Perioral BTX-A can be successfully used to improve the effects and duration of laser resurfacing, nonablative laser, light rejuvenation and perioral dermal fillers.

Mentalis (Chin) Puckering and Mental Creases

BTX-A is very successful at decreasing these particular lower facial movements. In most patients, a single injection into the center of the mentalis muscle of 4 to 6 U of Botox will be effective. This will usually avoid any undesirable effects on other lower facial muscles.10,15
Neck Lines and Platysmal Bands

This author is not convinced of the benefits of Botox for the horizontal “necklace lines.” I prefer to treat with nonablative laser or light rejuvenation and light to mid-strength chemical peels.\textsuperscript{10}

Vertical Platysmal bands are, in contrast very successfully treated with BTX-A.\textsuperscript{1,2,9} The patient is asked to hyperextend the neck (Figs. 1–2). Either the injections can be made into the extended platysmal bands which has the advantage of being grasped between finger and thumb and the needle inserted vertically into the muscle band. The dose is usually 2 to 4 U of Botox spaced 4 cm apart.\textsuperscript{9,10} See Figures 2 and 3 for pre (Fig. 2) and post (Fig. 3) BTX-A treatment of platysmal bands.

Some patients cannot hyperextend for sufficient time and here the bands are marked with skin marker at the sites for BTX-A injection and the BTX-A injected into the muscles at rest.

There have been suggestions that higher doses of Botox can be used for the neck.\textsuperscript{3} One problem that can result is dysphasia, dysphonia, and anterior neck weakness with high doses which are probably better avoided.\textsuperscript{9,16}

Lower Facial Contouring—Masseteric Injections of BTX-A

Recent observations have shown that the contour of the lateral cheek area can be flattened and the jaw line defined by injections of Botox to the Masseter muscle.\textsuperscript{17} This seems to be esthetically useful in the rounder-faced individuals and was described initially in a group of 45 Korean patients. Transient side effects included masticatory and speech disturbances.\textsuperscript{17}

Conclusions

Botulinum toxin for selected patients may be helpful for lower facial lines and aging. Doses usually are lower than in the upper face and any unwanted effects last longer. Combining BTX-A with other treatments such as dermal fillers, peels, nonablative and resurfacing treatments can be successful for lower facial and neck rejuvenation.

Lower Face and Neck Lines

Candidate sites for BTX-A with doses for Botox are:

- Perioral lines. The mucosal surface of the lips is anesthetized with 30% Benzocaine gel and inject through the mucosa (between 2 to 8 U per lip maximum dose).
- Marionette lines (downturning of the lateral lips). The lower part of depressor angular oris muscles is injected (usually 4 U per side).
- Platysmal bands (usually 8-12 U per band).
- Masseteric injection for lower face contouring (possible dose 30 U per side).

Treatment of these areas of the aspects of the lower face can then be successfully combined with laser resurfacing, nonablative laser, chemical peels, dermal fillers, lip implant and topical therapy.

Our technique for combining BTX-A with facial or perioral laser resurfacing is as follows:

1. Pretreat with BTX-A, ideally at least 2 weeks before laser skin resurfacing.
2. Postlaser treatment, BTX-A should be injected before the muscle activity causes a return of dynamic rhytides, this is usually 3 months after the first injection.
3. For ongoing treatment with the nonablative lasers (eg, CoolTouch, Pulsed Vascular Laser or Intense Pulsed Light (IPL)), repeat BTX-A injections three to four times over a 1 year period, thus allowing more efficient, smoother dermal connective tissue remodelling (studies are currently in progress to prove this theory).
4. For selected patients with neck aging, a combination of BTX-A with cool touch, vascular, IPL (for poikiloderma) or superficial resurfacing lasers can be very successful; however, excessive quantities of BTX-A should be avoided on the neck because of deeper effects on pharyngeal and laryngeal muscles.

References