Treatment of Hyperfunctional Lines of the Face with Botulinum Toxin A

WILLIAM J. BINDER, MD, FACS
ANDREW BLITZER, MD, DDS, FACS
MITCHELL F. BRIN, MD

Since Botulinum toxin A became a mainstay therapy for blepharospasm, its use in treating other dystonic conditions, spasticity disorders, as well as hyperfunctional lines of the face has increased exponentially in recent years. The following article summarizes our experience in establishing a safe and reliable method of administration of botulinum toxin A for treating hyperfunctional lines of the face © 1998 by the American Society for Dermatologic Surgery, Inc. Dermatol Surg 1998;24:1198-1203.

Over the last 13-14 years we have found an increasing array of medical uses for botulinum toxin. Originally discovered by Scott et al. as a treatment for strabismus and blepharospasm, botulinum toxin has become the standard therapy for many dystonic and spastic disorders. Since 1984, thousands of patients with focal dystonias have been treated utilizing botulinum toxin. Published reports by Blitzer and Brin et al. have reported their experience in treating blepharospasm, torticollis, oromandibular dystonia, adductor and abductor laryngeal dystonia, lingual dystonia, limb dystonia, and hemifacial spasm. A number of years ago, a new use was discovered by Blitzer et al., Keen et al., and Carruthers and Carruthers for the treatment of wrinkles and hyperfunctional lines of the face.

Excessively prominent facial lines are often cosmetically displeasing and sometimes misinterpreted as anger, anxiety, fear, fatigue, pain, sadness, or associated with aging. The many different surgical, medical, and cosmetic remedies that emerge and are marketed each year can be confusing to both the patient and the surgeon. Consequently, it is incumbent upon the physician to differentiate and choose the most appropriate treatment for each individual problem and patient. In general, facial rhytids have a myriad of remedies: facelift, surgical excision, implants, resurfacing procedures using either lasers, acid peels, or dermabrasion, soft tissue fillers such as collagen, fat, derma, or Gore-Tex, facial contours, facial massages, and other homeopathic remedies. Therefore, to choose the most appropriate therapy, distinctions must be made between rhytids created by loss of collagen or elastic fibers within the dermis of the skin, wrinkles caused by volumetric loss of fat, redundant folds caused by gravitational pull, and those caused by hyperfunctional facial muscles.

The three primary areas of the upper third of the face associated with hyperfunctional movement such as the glabella front line, horizontal forehead lines, or crow's feet historically have been resistant to most therapies. Even after myectomy via direct or endoscopic brow lift, the corrugator muscles and the secondary front lines have a high incidence of recurrence. Fuller agents such as collagen or fat often only a partial, short-term solution to fill and smooth out deep lines or folds. Direct excision may eliminate the line but, at the same time, also may leave unsightly scars. In the lower third of the face, a "pouc d'orange" effect or excessive wrinkling is often found over the anterior portion of the chin. This is caused by the hyperfunctional mentalis muscle, which is associated with labial incompetence in patients with retrognathia, micrognathia, or frequently after chin augmentation. It is also found more frequently in this area in older age groups. We have been able to significantly decrease or eliminate these lines by injecting the mentalis muscle with small amounts of botulinum toxin (approximately 2-4 U). The tensed skin is smoothed out and the effects of skin wrinkling caused by the excessive straining of the mentalis muscle is reduced. In the neck, the platysma muscle bands can also be reduced by a series of botulinum toxin injections into the anterior aspects of the platysma muscle bands. This usually requires approximately 2.5-5 U and three injection sites per side.

The basis for treating facial lines with botulinum toxin must address the etiology of the specific facial line. In hyperfunctional facial lines, such as the brow furrow, crow's feet, and horizontal forehead wrinkles, it
is the tension of the underlying mimetic facial muscu-
lature that causes a pleating of the overlying skin. Pa-
tients who have Bell's palsy have a functional disability of
the facial muscles, but also have smooth skin without
the development of deep hyperfunctional lines. In pa-
tients treated with botulinum toxin for facial dystonia or
hemifacial spasm, we observed a reduction or ab-
se of deep hyperfunctional lines with an improved
cosmetic appearance.5,20

**Botulinum Toxin: Mechanism of Action**

Botulinum toxin weakens the overactive underlying
muscle contraction, causing a relaxation and flattening
of the facial skin, which yields an improved cosmetic
appearance. The bacterium *Clostridium botulinum* pro-
duces eight serologically distinct toxins designated A,
B, C1, C2, D, E, F, and G.21 Botulinum toxin acts at
the neuromuscular junction, inhibiting the release of ace-
tylcholine from the nerve terminal. This causes weak-
ness or a flaccid paralysis of the muscle.

Pharmacologic and morphologic studies suggest the
toxin enters the nerve ending via endocytosis and in-
hibits the release of the vesicle-bound acetylcholine
within the nerve terminal itself.22-25 The therapeutic
effect thus is related to the peripheral blockade of neu-
romuscular activity, which causes muscular weakness.
So far there has been no evidence to suggest any per-
manent degeneration or atrophy of muscles in those
patients treated for dystonic or spastic disorders who
have been injected with high-dose, repetitive injections
of botulinum toxin over a long duration. Muscle bloo-
dis that were taken from patients after injections of
botulinum toxin two to five times those used for aes-
thetic improvement failed to show any long-term evi-
dence of permanent degeneration or atrophy.26,27

**Safety Issues**

There have been no long-term adverse effects or health
hazards related to the use of botulinum toxin thus
far.1,12-29 Patients receiving repetitive, high doses of
botulinum toxin have been shown to develop antibod-
ies to the toxin. These act as blocking antibodies and
may render the patient resistant to further treatment.
They do not cause hypersensitivity reactions to the in-
jection of the substance. The factors that predispose
patients to the development of antibodies are unknown,
but experience has shown that the risk is increased with
repetitive dosages above 300 U.13-14 Dosages for indi-
vidual sites treated for the purpose of minimizing hy-
perfunctional facial lines usually require no more than
20-40 U per site. To further minimize the dose and
increase the accuracy of toxin placement we often use an
electromyographic (EMG)-guided technique. Once

familiar with the origin and insertion of the facial mus-
cles, many of these areas can be injected with a 30-
gauge needle without EMG guidance. However, in
those patients who have shown only partial results
from prior treatments, we recommend that the EMG

techique be used to assure more accurate deposition of
the toxin.

In the informed consent, it must be brought to the
patient's attention that botulinum toxin has been ap-
proved by the Food and Drug Administration as a safe
and effective "on label" therapy since 1989 for use in
blepharospasm, strabismus, and hemifacial spasm.
The treatment of wrinkles is considered an off-label use.
However, the National Institutes of Health consensus
conference of 1990 also included botulinum toxin as
safe and effective therapy for the treatment of adductor
spasmodic dysphonia, cranial and facial dystonia, and
cervical dystonia.30 Other "off-label" uses include
Meige's syndrome, spastic dysphonia, tremor dis-
orders, juvenile cerebral palsy, and other spastic dis-
orders for which patients currently are receiving benefit
from botulinum toxin.

**Prior Study**

In a previous study,27 we reported the results of a series
of 210 injection sites in 162 patients. The patients had
preinjection and postinjection photographic documen-
tation and ratings on a four-point qualitative evaluation
scale of lines at rest and with action. The patients then
had botulinum toxin type A injections, via a monopolar
hollow-bore, Teflon-coated EMG needle, into the facial
muscles associated with the hyperfunctional lines.
The total dose for each region was 1.25-25 U divided into
1.25-5 U aliquots representing 0.1-0.2 ml per injec-
tion site, depending on the site and the prior experience
using toxin on that patient. Ninety-five percent of the
patients treated had cosmetic improvement of un-
sightly facial lines or contractions. The best results
were achieved in management of the forehead lines, followed
by glabella, upper feet, and nasolabial folds. The dose
for forehead lines was 5-25 U (mean 17.3 ± 6.2); gla-
 bella lines 5-20 U (mean 11.1 ± 3.1); crow's feet 5-15 U
(mean 6.2 ± 1.6); nasolabial folds 2.5-5 U (mean 3.12 ±
1.2); and platysma 10-20 U (mean 15 ± 4.0). Effects of
the toxin were seen 24-72 hours after injection and
lasted 3-6 months, whereupon the increased muscular
activity returns, as do the hyperfunctional lines. The
improvement in hyperfunctional lines utilized a 0-3
rating scale (0 reflecting no facial wrinkles, 1 signifying
mild facial wrinkles, 2 denoting moderate facial wrin-
kles, and 3 representing severe facial wrinkling at rest
and during function).

Patients had their re-evaluation at 2-3 weeks postin-
jection. Patients returned for additional follow-up when
The therapeutic effect diminished. Evaluation by age and site suggested a trend of increased toxin dose with increased age. The only morbidity was related to temporary mild weakness of orbicularis adjacent facial muscles. There were no systemic side effects. In addition to the cosmetic benefit, it was noted that several patients who suffered from either migraine or chronic headache pain had relief of their symptoms after the administration of botulinum toxin to the forehead, temporal, and/or glabellar regions (Binder, personal communication, 1994).

Initially, several nasolabial injections were given. Although they reduced the nasolabial groove, they also diminished the elevation of the lip for smiling, which was not an acceptable cosmetic outcome for most patients and was abandoned.

The adverse effects of the toxin injections were min-

![Figure 1. Injection technique. Mildly compressing the skin with one's finger against the margin of the superciliary rim further reduces the chances of extravasation of botulinum toxin beyond the intended area of injection site.](image1)

![Figure 2. Injection technique. Mildly squeezing the belly of the corrugator muscle between two fingers and lifting it superiority ensures more accurate placement of the toxin and its confinement to the muscle.](image2)

![Figure 3. Botulinum toxin is supplied in 100-U vials as a frozen concentrate that is reconstituted with preservative saline at various concentrations.](image3)

![Figure 4. A small electromyographic (EMG) machine with ground and reference leads and the Teflon-coated EMG needle with attached spring consisting of botulinum toxin. The Teflon-coated needle acts as the probe and delivery device.](image4)
imal and included seven patients who experienced temporary droop of the eyelid or eyebrow, or droop of the upper lip from nasolabial fold injections. No systemic reactions were noted. The effects of the injection lasted an average of 3–6 months, when most patients returned for re-evaluation and treatment. Subsequent to this study, specific techniques of injection utilizing precise placement of small volumes with slow injection of the toxin are important factors in preventing dispersion of the toxin outside the boundaries of the desired effect. In the glabella area, direct pressure at the border of the supraperiosteal space also reduces the potential for extravasation of botulinum toxin, avoiding inadvertent weakening of the levator muscle of the upper eyelid (Figure 1). In addition, by grasping the mid to lateral portion of the corrugator muscle between two fingers, the deposition of botulinum toxin into this area can be limited further and extravasation prevented (Figure 2). Over the past 4 years, by using these techniques, we have seen no ptosis of the upper eyelid in more than a 1,000 injections.

Figure 5. Between 10–20 U if botulinum toxin are injected over five injection sites over the glabella region.

Figure 6. Between 5–10 U of botulinum toxin are injected over three injection sites per side for crow’s feet.

For clinical use, the toxin is reconstituted with normal, nonpreserved saline to a concentration of 2–4 U/ml. If the EMG technique is used, the toxin is injected via a monopolar hollow-bore, Teflon-coated EMG needle connected to an EMG amplifier (Figure 4). Using previously described techniques, the needle is placed through the skin overlying or adjacent to the facial line and into the hyperfunctional muscle. Before placement of the needle, the patient is instructed to accentuate the specific facial expression, such as frowning, squinting, or elevating the eyebrows. Once the needle is inserted in the muscle, it may be moved slightly until it is in the most electrically active part of the muscle complex and produces the maximum EMG signal. The toxin is then injected in 0.1- to 0.2-ml aliquots, depending on the dilution used. By using an initial low dose, a graded weakening can be achieved over sequential visits. Small volumes also minimize spread to adjacent muscles, producing unwanted weakness. In the glabella area between 3–20 U are given in five injection points. These are located medially in the right and left glabellar folds laterally in the right and left corrugator muscle belly, and a single injection centrally into the procerus muscle. (Figure 5). Between 5–10 U of botulinum toxin is injected over three injection sites per side for the crow’s feet: one site in the upper portion of the crow’s feet below the lateral corner of the eyebrow.

Figure 7. The dosage and number of injections vary depending on the number of forehead lines. This can range between 30–90 U and 5–10 injection sites. Botulinum toxin is usually not injected below an oblique line drawn from the medial brow to a point at least 1 cm above the lateral aspect of the brow.
one site approximately 1 cm lateral to the lateral canthus, and one site approximately 1 cm inferior to the lateral canthus (Figure 6). The dosage and number of injections for forehead lines depend on the depth and number of lines. The dose may range from 20 to 40 U dispensed between 5-10 injection sites. To avoid brow ptosis or prevent the ability of the patient from raising the eyebrow, it is important not to inject the area of the forehead below an oblique line drawn from the medial eyebrow to a point approximately 1 cm above the lateral portion of the eyebrow (Figure 7).

As in all cosmetic surgical procedures, it is important that pretreatment photographs be taken of the area being treated during the hyperfunctional and relaxed state. Ideally, it is best to obtain postinjection photographs at approximately 3-4 weeks. Because not all patients will have an "all-or-none" phenomenon that results in complete elimination of the hyperfunctional lines, it is important that an accurate pretreatment assessment be made. The patient's expected degree of improvement will depend on this assessment. Calculating the patient's age and skin type into a formula for improvement will help predict the therapeutic effect and provide the patient with a more accurate preoperative informed consent. For example, patients who are in their 20s or 30s with relatively thin, smooth skin will predictably have almost complete elimination of the frown lines (Figure 8). However, in older patients who already have wrinkling of the skin at rest or in patients with thicker, oily skin, only a partial result can be expected (Figure 9). It is important to inform the patient that these wrinkles around and below the lateral canthus caused by passive elevation of the cheek will continue to remain after botulinum toxin treatments. Conversely, these same lines will be prevented from becoming worse during active contraction of these facial muscles.

After successive treatments over prolonged periods
of time, some patients indicated that the effects of botulinum toxin were prolonged. Although there is no scientific basis to support the concept of muscular atrophy, we have observed that perhaps a new behavior modification is developed whereby patients learn to avoid certain undesirable facial movements.

A thorough medical history, including medications and any prior facial plastic surgery, must be obtained before treatment. Any patient who has a history of sensitivity to toxin or has had a neuromuscular disorder such as myasthenia gravis or Eaton-Lambert syndrome should not be treated.

Discussion

Each facial rejuvenation procedure must address the etiology of the cosmetic problem it is trying to correct. Hyperfunctional lines of the face are the result of a functional pull of the underlying mimetic facial musculature. Botulinum toxin weakens the overactive underlying muscle contraction, causing flattening of the facial skin and an improved cosmetic appearance. Other facial lines, related to active skin changes or age-related loss of dermal elasticity, with a leathery of facial skin, may respond incompletely to the toxin and should be treated with other adjunctive modalities.

Botulinum toxin has several advantages in the management of hyperfunctional facial lines and can be used during a routine office visit, with minimal discomfort. The only potential morbidity is related to temporary mild weakness of adjacent facial muscles. Using the electromyograph in refractory cases with the specific injection techniques described, provides additional safety factors that allow for placement of the toxin directly into the more active portions of the muscle. Accurate placement requires minimal toxin deposition to effect a positive clinical response. These small dose and volume requirements are likely factors that are responsible for the very low incidence of morbidity along with a high rate of successful clinical effects (Figures 10–12).
Conclusions

It is our experience that botulinum toxin is a safe and important adjunctive technique for the management of patients with hyperfunctional facial lines. Additional studies and research are necessary to determine the exact mechanism of botulinum toxin on both nerve and the neuromuscular pathways in addition to investigating other adjuvants that can be used concurrently to achieve longer periods of benefit.

References