Clostridium botulinum was first identified as a toxin in 1895 when it was linked to the death of several people who had ingested raw salted ham. The ensuing investigation led to Botulinum toxin finally being purified in the 1940s in its most stable form, Type A exotoxin. By the early 1960s, ophthalmologists were investigating the use of Botulinum toxin for treatment of strabismus, culminating in clinical trials in the late 1970s and the discovery that Botulinum exotoxin A causes effacement of facial lines of animation. That discovery led to the use of Botulinum exotoxin over the past decade for the management of symptomatic lines of facial expression.

BTX-A is one of eight serologically distinct and the most potent neurotoxin produced by the anaerobic bacterium clostridium botulinum. It is received freeze-dried in a vial containing 100 units of toxin, 0.5 mg of human albumin, and 0.9 mg of sodium chloride. Each vial must be kept frozen until unpreserved sterile saline is added for reconstitution. The manufacturer recommends using the product within four hours of dilution; some clinicians refrigerate the unused portion and have used it seven to 30 days later.

BTX-A causes a temporary chemical denervation of the motor end plates of voluntary muscle by binding to the presynaptic neuron at the neuromuscular junction. Because there is ongoing turnover of the neuromuscular junction, the effect of BTX-A is transient, and muscle function gradually returns after three months.

General adverse reactions to injection of BTX-A can include ecchymosis, erythema, rash, headaches and general malaise. Site-specific complications occur because of diffusion of the solution to adjacent muscles. The maximum total recommended dose is 300-400 units at any one session and not more than 400 units over a three-month period; the LDo of humans is estimated to be 2730-3000 IU. Dose-related immunoreistance is potentially a concern with large doses or frequent drug administration (i.e., less than three months).

Therefore, to avoid potential complications it is recommended to: (1) use the smallest possible effective dose, (2) extend the interval between treatments (at least three months) and (3) avoid booster injections.
Patient Instructions After The Botulinum Injection

- Expect minimal redness, swelling or bruising at the injection sites.
- Avoid heavy physical exercise, lifting, bending or lying flat on back for a minimum of 4 hours post injection.
- Do not massage or rub the injection site for 24 hours.
- Make-up may be applied 4 hours after the procedure.

BTX-A is contraindicated in pregnancy, during lactation, in patients with sensitivity to human albumin, and in patients who are taking aminoglycoside antibiotics or any medication that may potentiate the effects of BTX-A. Individuals with pre-existing neuromuscular conditions or individuals experiencing symptoms of neurological or muscular diseases also should avoid use of BTX-A.

Techniques of Injection

Prior to injection, the patient may desire an oral anxiolytic, ice compresses or a eutectic mixture of local anesthesia. The treatment area is then cleansed with alcohol and the patient is instructed on how to activate the involved muscles. Superficial muscles (i.e. orbicularis oculi, orbicularis oris, and procerus) can be treated by subcutaneous or intramuscular injection of BTX-A. Larger or deeper muscles (frontalis, corrugator supercilii, levator labii superioris alaeque nasi, levator labii superioris, and platysma) can be treated by intramuscular injection. We prefer to use serial, multiple sites of injection into the muscles.

After injection, the assistant then applies gentle pressure to each area. Patients are instructed to remain upright and avoid manipulating the treatment site to avoid unwanted diffusion of the toxin to adjacent sites. By activating the muscle, patients can enhance local uptake of the toxin.

BTX-A is utilized for chemodenervation of hyperfunctioning facial muscles of animation that produce unwanted furrow or rhytids (lines, wrinkles). The mimetic facial muscles pull on the overlying skin causing lines or wrinkles perpendicular to the pull. The BTX-A weakens the hyperdynamic muscle action and improves the appearance of the skin.

Denervation may be observed a few hours or up to 14 days after treatment; therefore, “touch-ups” should be avoided for two weeks. The effects of the BTX-A are related to the volume of solution, the toxin dilution, the activity of the toxin, individual patient variation, and the number of injections at each site. Though muscle action begins to return at three months, patients subjectively determine the need for additional treatments at varying time intervals.

The procedure can be performed alone as an office procedure or added intraoperatively in conjunction with surgery.

Frown Lines

Corrugator supercilii muscle hyperactivity results in vertical glabellar furrows otherwise known as “11” lines. Transverse lines at the root of the nose are due to the action of the procerus muscle. We dilute the BTX so that there are five units per 0.1 ml of solution, and then inject 15-30 units (0.3-0.6 ml) of BTX-A into the involved muscle in divided doses, by serial injections. One should follow the anatomic distribution of the muscle and avoid crossing the mid-pupillary line.

The most significant complication associated with injection at these sites is upper eyelid ptosis due to migration of the toxin to the levator of the upper eyelid. Onset occurs at one to two weeks after injection and resolves within four weeks. Ptosis can be alleviated by using ophthalamic eyepatches containing alpha-adrenergic agonists, which stimulate Mueller's muscle and immediately elevate the upper eyelid, restoring it to a normal position. Commonly, apraclonidine 0.5 percent (Iopine, Alcon Labs, Fort Worth, Texas, and phenylephrine) (Neo-synephrine hydrochloride 2.5 percent, Sanofi, Winthrop Pharmaceuticals, New York, NY) are used requiring one to two drops three times a day and continued until levator function returns. Nafcon A (naphazoline hydrochloride 0.025 percent: phenyramine maleate 0.3 percent, Alcon Labs, Fort Worth, Texas) can also be used.

Forehead Lines

Transverse forehead rhytids secondary to frontalis muscle hyperactivity can be treated with approximately 25-50 units of BTX-A depending on the degree and extent of rhytids. The toxin is injected in a grid pattern across the forehead directly into the muscle. After discussion with patients, injection of the lateral brow is sometimes omitted to avoid the sensation of a heavy eyebrow due to the loss of the brow elevator muscle. Patients
are advised of the possibility of unusual arching of the lateral brow with frontalis animation if injection of the lateral brow is omitted. Alternatively, the entire frontalis can be injected and the antagonist orbicularis oculi injected with 2.5-5.0 units in the sub-brow position to counter the loss of elevator muscle function.

**Crow’s Feet - Squint Lines**

Crow’s feet develop from overactivity of the orbicularis oculi and are usually treated with a total 30 units or less of BTX-A for both sides. The patient is asked to squint and the lateral orbital rim is palpated, locating a position one fingerbreadth away from the rim. The injections are performed in 2.5-5.0 unit intervals in the subcutaneous plane, typically in the shape of an arc. Injection too close to the rim may affect the extraocular muscles and cause diplopia or lower lid ectropion.

“Ultimately, BTX-A has proved to be a safe and important technique for the management of patients with symptomatic lines of facial expression.”

**Vertical Neck Lines**

The platysma muscle is another suitable area for BTX-A treatment. Patients commonly complain of cords or a “turkey gobble” neck appearance that is due to hyperactivity of the platysma muscle. While the patient is forcefully grimacing, injections in aliquots of 2.5-5.0 units are injected into the muscle belly along the cord. The total volume used is usually between 50-100 units. Occasionally sequelae of injection at this site may include edema, erythema, muscle soreness, and neck discomfort. Two cases of dysphagia have been reported that resolved spontaneously by day 14.

Perioral lines, nasolabial folds, and the chin crease are other areas that have been treated with BTX-A by some clinicians. 1.0-1.5 units of BTX-A has been used for the vertical perioral lines that originate from the vermilion border. Overzealous use has lead to weakness of sphincter tone around the mouth. Using up to a total of 5-10 units for the nasolabial folds has helped soften the appearance of the medial aspect of the nasolabial fold but can cause lip drop and is thought best suited for patients with long face syndrome and prominent nasolabial lines. Injections of the mentalis muscle have improved the appearance of the chin crease but may result in labial incompetence.

The paralysis induced by the BTX-A can be a useful adjunct to other aesthetic procedures including soft-tissue fillers/augmentation and with laserabrasion where reduction in motor activity enables a more even distribution of new collagen formation.

Ultimately, BTX-A has proved to be a safe and important technique for the management of patients with symptomatic lines of facial expression. Its benefits are achieved by deactivating the involved muscle of facial expression and causing an effacement of the overlying skin. Furthermore, BTX-A can be used to alter the activity of counteracting muscles of the face to harness the imbalance that is created.

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**References**


