Aesthetic Uses of Botulinum Toxin A

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Since 1987, botulinum toxin A (BTA) has been used to denervate certain muscles of facial expression that are in part responsible for static facial rhytids. It has been applied to rhytids in the glabella, forehead, lateral canthal skin, and neck. Additional uses in oral and maxillofacial surgery include the denervation of hypertrophic or hyperactive masticatory muscles for cosmetic and functional purposes.

This article reviews the biochemical and physiologic properties of BTA, its preparation, applications to oral and maxillofacial surgery in terms of treatment options and techniques, and potential complications. A standardized measurement technique is also described that avoids the treatment variables that may produce unwanted effects of BTA.

Preparation and Storage

BTA is sold under the name of Botox (Allergan, Irvine, CA) and is available in 100-unit vials of lyophilized toxin that must be reconstituted before use. The toxin is prepared for usage by adding 1.2 mL unpreserved sterile saline to the vial. The vial is gently rolled in the hands to mix the solution, because shaking or frothing can inactivate the toxin. Once prepared, the solution is drawn up in separate tuberculin syringes each containing 0.35 mL or 29 units, of BTA. These syringes are stored on ice in the refrigerator until usage.

Techniques

All patients are queried about pregnancy or contraindicating factors and sign a treatment consent. Preoperative photographs are made on all patients in repose and in animation. The patients are advised to remain vertical for 4 hours after injection and to refrain from strenuous activity that day.

GLABELLA

The most common site for cosmetic injection of BTA is the glabellar region. Facial rhytids and folds in this area are a result of the action of the depressor muscles (orbicularis oculi, corrugator supercilli, and procerus) (Fig 1). The following injection technique has proved predictable in avoiding unwanted lid ptosis or extraocular muscle paralysis.

The corrugator, orbicularis oculi, and procerus muscles are injected with 0.05-mL aliquots (4.15 units) of BTA in previously marked injection sites. Measurements are made with the patient seated upright and relaxed, and bilateral markings are made on the skin with a surgical marker 1 cm above the bony orbital rim in the midpupillary region and medial canthal regions to reference the injection sites (Fig 2). After an alcohol skin preparation, the first and second injections are performed through the same puncture site. Asking the patient to scowl flexes the corrugator musculature, and the resultant skin bulge can be palpated. A 0.5-inch, 30-gauge needle is inserted through the skin at a 45° angle to approximately one half to three-fourths of the needle depth in the medial brow landmark, and 0.05 mL is injected (Fig 3A). This inactivates the corrugator supercilli muscle. The syringe is withdrawn without exiting the skin and redirected perpendicular to the skin surface (Fig 3B). The needle is then advanced to bone and withdrawn to approximately one half of its length, and the next aliquot of 0.05 mL is injected into the superiomedial portion of the orbicularis oculi muscle.

Attention is then focused on the central brow mark above the midpupil. The needle is inserted to the level of bone and withdrawn to one half its length, and a 0.05-mL aliquot is injected (Fig 3D). This injection will paralyze the superior central portion of the orbicularis oculi muscle while still maintaining normal orbicularis function.

The final injection is directed into the center of the procerus muscle at the mark between the eyes. The needle is inserted into the nasal bridge to one half of its length, and 0.05 mL is injected (Fig 3C). Figures 4 and 5 show successful treatment of glabellar wrinkling. The patients are trying to produce the same scowl in both pictures.

FRONTALIS REGION

If the surgeon wishes to impair frontalis function, the injections may be combined with the glabellar treatment or done separately. A smaller dose of BTA is used in this region. The patient is asked to raise the

FIGURE 2. Specific injection sites for BTA injection in the glabellar region. Seven injections are made in the following order: Injections number 1 and 2 are made through the same puncture site and treat the left corrugator and medial orbicularis. Injection number 3 treats the left superior central orbicularis. Injections 4 and 5 are also made through the same puncture site and treat the corrugator and medial orbicularis on the right side. Injection number 6 treats the superior central orbicularis on the right side, and injection number 7 treats the procerus muscle.

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FIGURE 72 hours postinjection of BTA for hyperfunctional glabellar lines.

eyebrows, and the skin bulges are noted. Three to five 0.025-mL injections (2.1 units) are performed along the horizontal fold, depending on its width. Only the most superior folds are treated, allowing the inferior portion of the frontalis to maintain its function of elevation of the brows.

When treating the entire frontalis region, 6 to 12 injection sites are used, depending on the horizontal width of the wrinkles (Fig 6). If the wrinkles extend to the temporal region, lateral injections are also performed, with caution not to inject lateral to the lateral canthus so as not to affect the temporalis function. Figure 7 illustrates the successful treatment of frontalis wrinkling. This is the same patient pictured in Figure 6. Note the preservation of eyebrow elevation in the preinjection and postinjection photographs, resulting from sparing of the inferior frontalis fibers.

LATERAL CANTHAL RHYTIDS (CROW’S FEET)

The effects of contraction of the lateral aspect of the orbicularis oculi contribute to the hyperfunctional lines in the lateral canthal area. These wrinkles are accentuated when squinting or smiling. To treat this area, a measurement is made 1 cm lateral to the orbital rim, and the skin is marked. The skin is prepared with alcohol, and the area is injected with 0.025 mL (2.1 units). The area of greatest folding several millimeters directly above and below the initial injection site is also injected, for a total of 6 units per side (Fig 8). If the patient is recruiting muscle fibers lateral to the lateral canthus, this area also requires injection to provide a good clinical result. This must be done carefully because injections placed more than 1 cm lateral to the orbital rim may affect temporalis or mimetic muscle function. Injections are not performed closer than 1 cm from the lateral orbital rim to prevent diffusion into the orbit.

MASSETERIC HYPERTROPHY

The patient is seated in the upright position and asked to clench the teeth. The greatest area of bulge is palpated, and 0.025 mL (2.1 units) is injected into the muscle bulge. This is performed in the most obvious areas, and the patient is asked to return on a weekly basis to treat to a symmetrical end point. Figure 9 shows successful reduction of masseteric hypertrophy after 2 sessions of 4 injections each.

FIGURE 5. Preinjection and 72 hours post-BTA injection for glabellar wrinkles and folds.
FIGURE 6. Areas of the frontalis muscle injected for hyperfunctional lines and folds. Note that the most inferior muscle bulge is not treated to maintain eyebrow elevation.

COMPLICATIONS

Seventy patients were treated (some of them multiple times over 19 months) for a total of 112 total BTA patient treatments consisting of approximately 1,200 BTA injections over the 19-month period. No complications were seen in this series when adhering to the measurement schemes and injection techniques described. The main complication that can be encountered is unwanted paralysis of the surrounding musculature. A 1% to 2% incidence of levator palpebrae superioris ptosis manifested by a ptotic eyelid has been reported. Ophthalmoplegia has also been reported. A single case of unilateral upper eyelid ptosis was encountered in this series, before the measuring technique was developed, and this was treated with an alpha-adrenergic agonist (Iopidine 0.5%; Alcon Labs Inc, Fort Worth, TX), which stimulates the sympathetic musculature and temporarily elevates the ptotic lid. The ptosis spontaneously resolved in 28 days.

To avoid unwanted paralysis, the solution should be injected slowly, without undue pressure, and not inadvertently injected into undesirable regions.

Discussion

Botulinum toxin A (BTA) is one of the 8 exotoxins produced by the bacterium Clostridium botulinum. It is a neurotoxin and causes its effects on the neuromuscular junction by inhibiting the release of acetylcholine (ACH), causing weakness or flaccid paralysis. The storage or synthesis of ACH is not affected by BTA, but its action affects the vesicle-bound ACH. It binds specifically to cholinergic motor endplates and blocks the release of ACH from the presynaptic vesicles, causing neuromuscular blockade. The binding of the molecule to the motor endplate is permanent, and it takes 24 to 48 hours for the therapeutic condition of weakness or paralysis to ensue because of this chemical denervation. The reason for this delay is the time required for the storage vesicles of ACH in the presynaptic motor endplate to be depleted. Although the binding of the ACH is permanent, the paralytic effect only persists for 2 to 6 months. The reason for this temporary action is the formation of new axonal sprouts, thus reestablishing the neurotransmitter pathway. This process of neoneurogenesis allows complete recovery of the transmission pathway and resultant muscle function.
First used in humans in 1973, small doses (35 to 50 units) BTA have been shown to be a safe and effective treatment for hyperfunctional lines and facial rhytids. The median lethal dose (LD_{50}) of BTA for humans has been calculated to be 2,500 to 3,000 units. The treatment dosage for facial cosmetic procedures is approximately 1/100th of the LD_{50}; therefore, an extremely safe therapeutic index exists.

Contraindications to the use of BTA include hypersensitivity to any component of the preparation, including human albumin. The use of aminoglycoside or spectinomycin antibiotics are known to affect neuromuscular transmission and can potentiate the paralysis associated with BTA. In addition, systemic neuromuscular diseases are a contraindication to the use of BTA.

The onset of paralysis usually takes a maximum of 72 hours. Several patients in this series experienced a subtotal paralysis and were reinjected 7 days later. The duration of paralysis has persisted up to 6 months, although most patients will regain muscle function within 4 months. The concentration of the solution, accuracy of the muscle injection, and individual susceptibility and variation in metabolism may affect longevity of the paralysis. Patients with thick, acneic, or oily skin may not show as dramatic a result and may require more aggressive treatment. Persons older than 65 years of age also may show a diminished response to treatment.

Although the manufacturer of Botox recommends that the solution be used immediately, storing the reconstituted solution in a standard refrigerator has not shown any attenuation of the clinical effects or duration. In the series treated, the reconstituted solution was commonly stored for 3 to 10 days.

BTA frequently was used several weeks before a chemical skin peel or laser resurfacing. Because the facial rhytids and folds were less prominent at the time of the resurfacing procedure, less aggressive laser treatment was needed in the glabellar, forehead, and lateral canthal regions, thereby reducing depth-related laser complications. In addition, the paralysis in these areas may allow a faster healing response, because animation disrupts the healing. Finally, paralysis of these muscles may, in theory, prevent the formation of new or deeper rhytids by preventing the repetitive creasing of the skin.

An incidental finding was that many patients experienced mild to moderate brow elevation when the glabellar region was treated. This presumably was a result of the frontalis muscle, the action of which was previously opposed by the depressor musculature. Some patients also exhibited folds or wrinkles in repose as well as animation before treatment. When treated with BTA, the wrinkling no longer persisted in repose, indicating that in some persons an uncon-
scious resting muscle tension or hyperfunctionality exists and that this responds to BTA treatment.

The patient acceptance of BTA treatment was unanimously favorable. They all appreciated the almost immediate and striking results and frequently returned for retreatment when animation recurred. The only drawbacks to further treatment were the cost of the BTA and the nonpermanent nature of the treatment.

As the use of BTA has become more prevalent, new aesthetic applications are evolving. BTA is now being used for the treatment of vertical lip lines, flaring nasal alae, platysmal banding, and to soften the nasolabial folds. Unwanted paralysis is the biggest drawback, and the results have been variable and less predictable than in the previously described anatomic areas.

References