

Botulinum Neurotoxin Type A-ABO (*Dysport*): Clinical Indications and Practice Guide

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The key points to remember about abobotulinumtoxinA are as follows:

- BoNTA-ABO (abobotulinumtoxinA [*Dysport*]; Medicis Aesthetics, Scottsdale, AZ) and BoNTA-ONA (onabotulinumtoxin A [Botox Cosmetic]; Allergan, Irvine, CA) are both derivatives of botulinum toxin A produced from different strains of the bacterium *Clostridium botulinum* through proprietary manufacturing processes, and both are approved by the US Food and Drug Administration (FDA).
- BoNTA-ABO and BoNTA-ONA, which are both type A botulinum toxins, should be further differentiated from Myobloc (Solstice Neurosciences, San Francisco, CA), which is the only FDA-approved type B botulinum toxin.
- BoNTA-ABO, as with other derivatives of botulinum toxin, produces a chemodenervation of the muscle by preventing the release and binding of acetylcholine at the neuromuscular endplate.
- The paralytic effect of BoNTA-ABO, as with other derivatives of botulinum toxin, produces a relaxation of the underlying muscle with the associated benefit of reducing dynamic rhytids of the overlying skin.
- BoNTA-ABO units are not interchangeable with BoNTA-ONA units. An understanding of the proper dosing and familiarity with the use of either botulinum toxin in aesthetic applications is required to produce results that are both safe and consistent.
- Spread of the toxin is dependent on solution volume and injection technique (physically pushing the toxin from the area of injection). Diffusion of the toxin is largely dependent on toxin dose and receptor concentration; unbound toxin moves down a concentration gradient.
- Beyond the treatment of glabellar rhytids, there are few, if any, randomized, double blind, placebo-controlled studies on the aesthetic uses of BoNTA-ABO. This guide summarizes what is known and serves as a basis for clinical use and continued understanding. (*Aesthet Surg J*;29:572-579.)

AbobotulinumtoxinA (BoNTA-ABO [*Dysport*]; Medicis Aesthetics, Scottsdale, AZ) is a potent neurotoxic agent used clinically in subtoxic doses, to target underlying muscle activity in an attempt to improve dynamic rhytids of the overlying skin. At the physiologic level, BoNTA-ABO produces a temporary chemical denervation of the muscle through the inhibition of acetylcholine release from somatic and autonomic nerve terminals. This results in reduced muscle strain and decreased production of facial rhytids during animation. The goal in the aesthetic patient, in addition to wrinkle reduction, is to produce a new “balance” in facial dynamics between agonist and antagonist muscle groups.

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Many changes associated with the aging face can be attributed to underlying muscular activity, muscle hypertrophy, and patterns of facial expression. However, aging also leads to the loss of skin elasticity and dermal support. The loss of subcutaneous fat and the pull of gravity lead to progressive ptosis of facial skin and soft tissue. When using BoNTA-ABO, as with other derivatives of botulinum toxin, a balance must be achieved for treating hyperactive muscles while still maintaining facial expression and minimizing facial ptosis.

PATIENT SELECTION

Patients with hyperactive corrugator and procerus muscles leading to dynamic glabellar lines are ideal candidates for BoNTA-ABO. The off-label applications of BoNTA-ABO include hyperactive frontalis muscle leading to transverse forehead rhytids, orbicularis oculi muscles leading to crow’s feet, nasalis muscle leading to “bunny lines,” mentalis muscle leading to dimpling, platysma

muscle leading to vertical bands, and axillary sweat glands leading to hyperhidrosis. Just as with other derivatives of botulinum toxin, new and creative uses for BoNTA-ABO are expanding greatly.

INDICATIONS

BoNTA-ABO achieved initial approval from the US Food and Drug Administration in April 2009. However, outside of North America, BoNTA-ABO has been used for therapeutic indications since 1991 and for aesthetic indications since 2001. Approved indications for BoNTA-ABO include “the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain in both toxin-naïve and previously treated patients” and “the temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients less than 65 years of age.”¹ Aesthetic uses of BoNTA-ABO have expanded to include those similar to BoNTA-ONA (onabotulinumtoxinA [Botox Cosmetic]; Allergan, Irvine, CA), including the targeted treatment of facial expression muscles in the forehead, periocular, nasal, perioral, mental, and neck regions.² BoNTA-ABO is also used in the treatment of axillary hyperhidrosis and migraine headaches.

While both BoNTA-ABO and BoNTA-ONA are type A toxins, an acute awareness of differences in dosing between BoNTA-ONA and BoNTA-ABO is essential, because 100 units of BoNTA-ONA do not equal 100 units of BoNTA-ABO. The units are not interchangeable. This is because of differences in the strain of bacteria, manufacturing process, and resultant complex size, not an inherent inferiority or superiority of either product. In general, BoNTA-ABO is less active on a unit-per-unit comparison with BoNTA-ONA, which means that more units of BoNTA-ABO are required to achieve similar effects. Therefore, BoNTA-ABO is packaged with more units per vial (300 units of BoNTA-ABO vs. 100 units of BoNTA-ONA). With normalized clinical dosing, similar results can be achieved as those with BoNTA-ONA. Indeed, some studies (including those with electromyographic evidence) show that BoNTA-ABO may achieve a clinical effect faster and maintains results longer when compared to BoNTA-ONA.^{3,4} Finally, some clinicians have raised the concern of BoNTA-ABO’s smaller complex size, which might lead to a higher risk of diffusion. However, studies show that the toxin quickly dissociates from the complex under physiologic conditions once it is injected, precluding complex size from resulting in differences in diffusion.⁵ Diffusion is attributable to the total dose and receptor concentration because the toxin moves down its concentration gradient. Spread is dependent on the volume injected and the injection technique; injecting a higher volume leads to increased physical distribution of the product as the fluid is pushed through the tissues from the point of injection.

A contraindication to BoNTA-ABO, just as with other botulinum toxin derivatives, is the presence of preex-

isting neuromuscular disorders that may lead to increased risk of severe dysphagia and respiratory compromise in those patients. No studies have been performed with drug interactions. However, care should be taken when administering BoNTA-ABO in patients taking aminoglycosides or anticholinergic medications, or in those patients with previous hypersensitivity to botulinum toxin products. In addition, muscle relaxers taken before or after BoNTA-ABO administration may potentiate muscle weakness. In the absence of well-controlled studies of BoNTA-ABO in pregnant women, BoNTA-ABO is not recommended during pregnancy or during nursing. The preparation of BoNTA-ABO contains lyophilized abobotulinumtoxinA, 125 mcg of human serum albumin, and 2.5 mg of lactose, with trace amounts of cow’s milk proteins. Those patients who are allergic to cow’s milk proteins (distinct from patients who are lactose intolerant) should refrain from using BoNTA-ABO.¹ Finally, a relative contraindication (not specific to BoNTA-ABO, but injections in general) is the use of blood thinning agents such as aspirin, ibuprofen, clopidogrel bisulfate, or warfarin. The most common side effect in these patients is an increased chance of bruising after injection.

PRETREATMENT PREPARATION

If a patient is deemed to be an appropriate candidate for BoNTA-ABO injections, he or she can be scheduled for the procedure. The risks, benefits, patient expectations, realistic results, and possible complications should be discussed with the patient before treatment, and an informed consent form should be signed and placed in the chart. Previous botulinum toxin use should be discussed and photographs can be taken of the patient in both relaxed and animated poses. Depending on the site to be injected, standard pretreatment photographic views include: (1) a neutral pose to document static rhytids and eyebrow position; (2) “frowning” to evaluate dynamic glabellar rhytids from procerus and corrugator muscle contraction; (3) “eyebrow elevation” to evaluate for dynamic forehead rhytids from frontalis muscle contraction; (4) “squeezing” the eyes closed to evaluate for crow’s feet from orbicularis oculi contraction, with additional oblique views to better visualize the lateral periorbital region; and (5) “grimacing” face to evaluate for vertical bands from platysma muscle contraction.

Ideally, we prefer that the patient returns two weeks later for posttreatment photographs, which we include in the medical record. Realistically, however, most patients do not return for three to four months—when the toxin is wearing off and it is time for their next injection. The patients who do return at the two-week mark are often those who perceive a problem or are requesting a touch-up. It is for these patients that the pretreatment photographs are crucial. For the majority of patients, comparing the pretreatment photographs with their posttreatment results relieves any concern about a problem with the

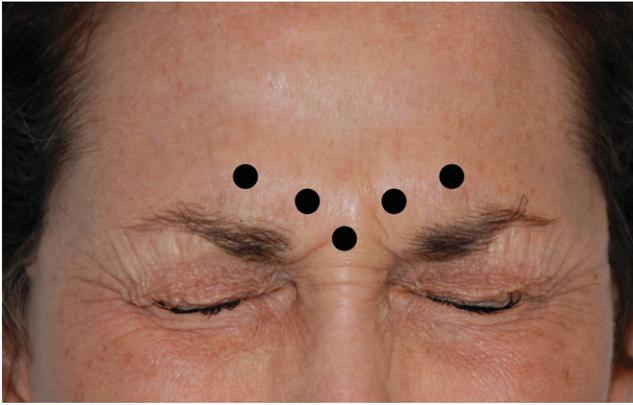


Figure 1. Glabellar injections are spaced approximately 1 cm apart for a total of five injections of 10 units each.

injection. If indicated, we avoid performing any additional injections within two weeks of the initial injection to allow the toxin to completely diffuse and achieve its full effect. It is important to avoid the temptation for early reinjection to prevent overtreatment.

When injections are properly done in appropriate candidates, therapeutic failures often are the result of one of the following cases: (1) a misunderstanding of the intended effect, (2) the recruitment of surrounding muscle, and (3) dermal atrophy with deep rhytids in absence of muscular activity.

Patient Preparation

The patient is seated in a relaxed position in an examination chair. The chair is reclined to approximately 60°, which allows the patient to lie back and stabilize his or her head while maintaining a vertical body orientation. In this position, the injector can continually evaluate brow position and natural facial animation during the injection process. The chair height is adjusted so that the top of the patient's head is approximately at shoulder level with the injector. This allows for the most comfortable and stable position of the injector's hand. If the patient requests numbing medication, we typically use a topical anesthetic cream, allowing sufficient time for adequate anesthesia. However, most patients do not require any medication pretreatment. In practice, quick dermal punctures (with prevention of past-pointing into periosteum or deep structures) combined with slow injection (to minimize pain from volume distention in the tissue) leads to minimal patient discomfort.

Markings

A new injector may feel more comfortable marking the intended injection points. However, with experience, this often becomes unnecessary. Our typical injection points for BoNTA-ABO are similar to those for BoNTA-ONA.² The most common area is the glabella (procerus and corrugator muscles). Five injection points are spaced approximately 1 cm apart in a "V" pattern (Figure 1), as described in the BoNTA-ABO package insert.¹ However,



Figure 2. Comparison of the packaging of BoNTA-ONA (Botox Cosmetic; Allergan, Irvine, CA) and BoNTA-ABO (Dysport; Medicis Aesthetics, Scottsdale, AZ). Botox Cosmetic is supplied in 50- and 100-unit vials. Dysport is supplied in 300-unit vials.

discretion must be used and individual adjustments made to accommodate for muscle bulk, severity of rhytids, variations in anatomy, and intended outcome in each patient. Additional off-label sites for aesthetic injections include the frontalis muscle, orbicularis oculi muscle, nasalis muscle, depressor septi nasi muscle, masseter muscle, orbicularis oris muscle, depressor anguli oris muscle, mentalis muscle, and platysma muscle. Except for the glabella, there are few, if any, randomized, double-blind, placebo-controlled studies on BoNTA-ABO dosing. Table 1 summarizes the BoNTA-ABO dosing information found in the literature and the guidelines from the manufacturer. Keep in mind that because BoNTA-ABO was only recently approved for use in the United States, there is limited experience to definitively outline off-label dosing recommendations.

Toxin Preparation

The BoNTA-ABO toxin is shipped overnight on ice from Medicis Aesthetics. It should be protected from light and refrigerated at 2°C to 8°C (36°F–46°F) until it is used. It is packaged individually in 300-unit vials, as compared to the 50-unit and 100-unit vials of BoNTA-ONA (Figure 2). The flip-top box provides easy access to both the vial and the package insert (Figure 3, A-D). As opposed to BoNTA-ONA, which appears as dust at the bottom of the vial, BoNTA-ABO appears as a powder cake at the bottom of the vial.

With your initial order, Medicis Aesthetics provides a simple pocket card outlining the dilution recommendations (Figure 4). Dilution with 0.9% sterile, preservative-free saline to the desired concentration is recommended (Table 2). *It cannot be overstated that BoNTA-ABO units and BoNTA-ONA units are not interchangeable.* It is unclear at this time, but a generally conservative rule of thumb is a x 1.5 to x 2.5 conversion ratio when mentally calculating BoNTA-ABO units from BoNTA-ONA units. However, one must keep in mind that every patient responds differently and that there is no universal dosage applicable to all patients or anatomic locations. The conversion may also not be along a linear curve. Specifically,

Table 1. Dosing recommendations for BoNTA-ABO (*Dysport*)*^{1,3,4,6-23}

Location	Dose
Glabella (procerus and corrugator muscles)	50 to 80 units divided into five areas 1 cm apart, keeping 1 cm above the supraorbital ridge; adjusted for sex and muscle mass
Forehead (frontalis muscle)	30 to 60 units divided into three to six areas, 1 cm apart
Crow's feet (orbicularis oculi muscles)	40 to 60 units divided into four to six areas, 1 cm lateral to the bony orbit
Brow "lifts" (orbicularis oculi)	10 to 12 units 0.5 cm above orbital rim in the lateral fibers of the orbicularis oculi muscle. Treat forehead depressors and avoid elevator muscles.
Lower eyelid rhytids (orbicularis oculi muscle)	Two to four units total, injected at the midpupillary point in two separate injection points
Gummy smile (levator labii superioris alaeque nasi muscle)	Three to seven units per side
Bunny lines (nasalis muscle)	Six to 15 units divided in two points on either side of the nose; additional three to five units centrally if necessary
Vertical lip rhytids (orbicularis oris muscle)	Two to six units at two or four injection points
Marionette lines (orbicularis oris muscle)	20 units per side divided into two injections per side, keeping at least 1 cm lateral from corners of mouth
Chin (mentalis muscle)	10 to 20 units in one site or separated into two sites
Masseteric muscle hypertrophy (masseter muscle)	100 to 300 units per side, divided in three into four areas within the muscle bulk
Platysmal bands (platysma muscle)	40 to 80 units per band, divided into four to eight injections per band, with each injection separated by 1 to 2 cm
Primary hyperhidrosis (sweat glands)	20 units at six sites, for a total dose of 120 units or 10 units at 28 sites for a total dose of 280 units

*These are preliminary recommendations compiled from data in the references listed in the table's title. These are (A) not intended for reproduction and (B) not a substitute for BoNTA-ONA (Botox Cosmetic) dosing.

varying doses may be required depending on the target tissue, receptor concentration, and physiologic condition of the patient—all of which may be unpredictable. Specific dosing for individual patients must be customized based on the patient's muscle bulk, severity of rhytids, and previous results with toxin injection. Higher dosing ratios have been suggested, but there is still uncertainty. In addition, many studies have been based on the medical indication for treating cervical dystonia, which involves much higher doses injected into much larger muscles. Dosing is an unresolved issue that may achieve clarity as more clinical experience is gained and well-designed scientific studies are undertaken. In the clinical setting, careful record keeping with specific dosages and anatomic locations can help fine-tune future

injections to match the patient's expectations and maximize outcome.

The product is reconstituted using an aseptic technique. The desired quantity of 0.9% sterile, preservative-free saline solution is drawn up with a 1-inch, 18- or 22-gauge needle in a 1- or 3-mL Luer Lok syringe and injected through the rubber stopper into the vial. The vial accommodates a maximum of 3 mL of diluent. The vial should then be swirled gently to avoid foaming, which can denature the product. The solution should be clear, colorless, and free of particulate matter. The solution is then drawn up with a 1-inch, 18- or 22-gauge needle into 1- or 3-mL Luer Lok or 0.3 mL ultrafine graduated syringes. The needle is then replaced with a 30- or 32-gauge 0.5-inch needle before

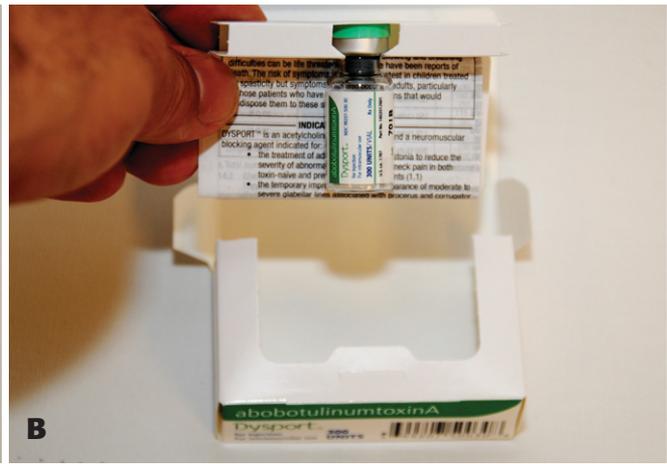
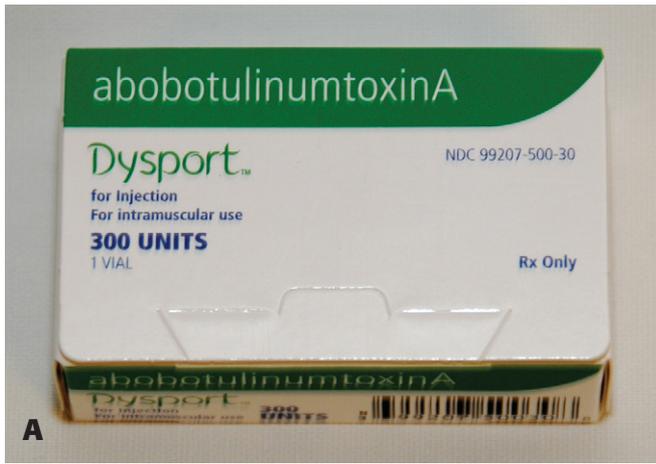


Figure 3. A, BoNTA-ABO (*Dysport*; Medicis Aesthetics, Scottsdale, AZ) packaging. Each vial is placed in an easily accessible flip-top box (B) with a hologram proof of purchase. C D, Each box contains a 300-unit vial of product.

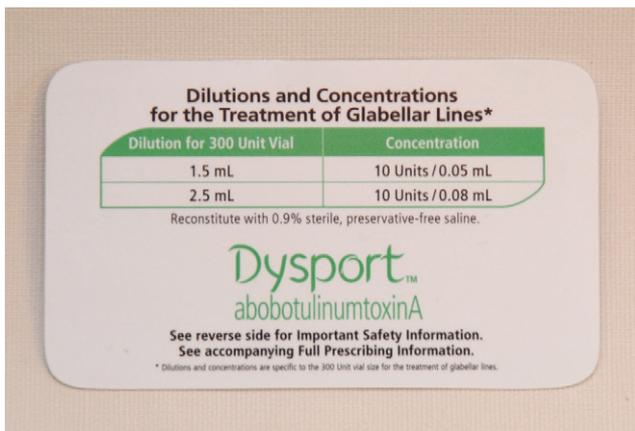


Figure 4. BoNTA-ABO (*Dysport*; Medicis Aesthetics, Scottsdale, AZ) pocket card, which outlines reconstitution and safety instructions for BoNTA-ABO.

injection. Frequent needle changes may be helpful in order to reduce patient discomfort from dull needle tips. However, changing needles prolongs the procedure and often is not necessary if one avoids past-pointing into the underlying bone. An alternative reconstitution procedure includes using a bottle opener to remove the vial's cap and rubber stopper. The saline can then be directly dripped into the open vial and the reconstituted solution drawn up into the syringe. When using this technique, one must remember that the vial contents

Table 2. Reconstitution of BoNTA-ABO (*Dysport*) and BoNTA-ONA (Botox Cosmetic)*

Type of botulinum toxin	Concentration (units/mL)
<i>Dysport</i> 300-unit vial	
1 mL	15/0.05
1.5 mL	10/0.05
2.5 mL	10/0.08
3 mL	10/0.1
Botox Cosmetic 100-unit vial	
4 mL	2.5/0.1
2.5 mL	4/0.1
2 mL	5/0.1
Botox Cosmetic 50-unit vial	
1 mL	5/0.1
2 mL	2.5/0.1

*Of note, BoNTA-ABO and BoNTA-ONA are not equivalent on a unit-to-unit basis. Care must be taken to assure proper dosing of each product. Specific dosing for individual patients must be individualized based on the patient's muscle bulk, severity of rhytids, and previous results with toxin injection.

are no longer sterile once the cap has been removed. Injections would then proceed as described.

It is recommended that the product be used within four hours of reconstitution, refrigerated at 2°C to 8°C (36°F–46°F), and protected from light until it is used.

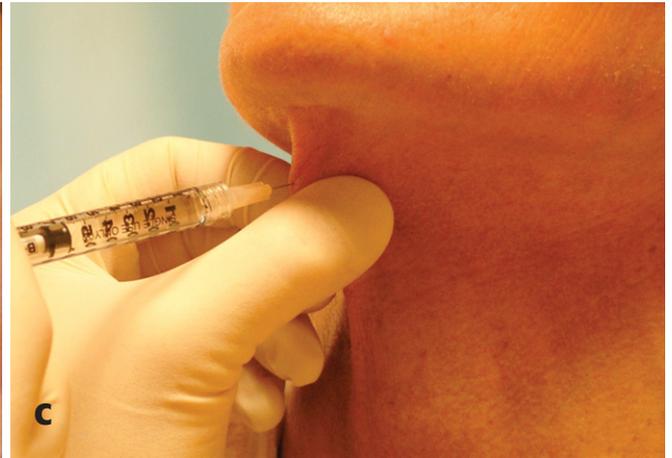


Figure 5. A-C BoNTA-ABO (*Dysport*; Medicis Aesthetics, Scottsdale, AZ) injection techniques are shown. Specifically, the target muscle is stabilized or grasped before injection.

As long as the rubber stopper has not been removed and the solution remains clear, colorless, and free of particulate matter, it can be stored for longer periods of time and remain clinically effective. However, because the product does not contain an antimicrobial agent, from a microbiologic point of view the storage of reconstituted product remains controversial and beyond FDA guidelines.

TREATMENT TECHNIQUE

The injection technique for BoNTA-ABO is essentially identical to BoNTA-ONA injections.² After suitable preparation, the muscles of concern are identified and isolated. The target muscle is stabilized or grasped (Figure 5, A-C) with the clinician's nondominant hand. Sequential injections then proceed as planned. Gentle pressure with gauze after injection can help reduce oozing and minimize swelling and bruising. We often inject the patient's left-side crow's feet first from the patient's left side, followed by the right-side crow's feet, glabella, and frontalis muscles from the patient's right side. All additional injections can also be completed from the right side. If the injector is left-handed, the order may be reversed. This order minimizes movement of the injector back and forth during the injection process. Before the first injection, any air

bubbles are expelled from the syringe and needle. Otherwise, the first injection may deliver a suboptimal aliquot of product if it is mixed with residual air bubbles residing in the Luer Lok or hub of the needle.

In most cases, the needle is inserted at a 90° angle into the bulk of the muscle, unless a different angle is required for precise anatomic localization of the target muscle. Injections proceed in a perpendicular fashion into the noncontracted muscle. Depth of injection depends on the muscle group. Direct muscle body injections are indicated for corrugators and platysma muscle, deep subcutaneous injections for frontalis muscles, and superficial injections for orbicularis oculi muscles. We prefer a serial puncture/high concentration (microinjection) technique rather than large bolus injections, to help prevent spread of the toxin. Unlike BoNTA-ONA, which is typically injected in 2.5- or 5-unit aliquots, BoNTA-ABO is typically injected in 10-unit aliquots at intervals approximately 0.5 cm to 1.5 cm apart. Dose and spacing depend on the underlying muscle, patient anatomy, previous patient response, and the intended result. Recent studies show that muscle bulk and patient sex should also be factored into BoNTA-ABO dosing, with male patients and bulkier muscles requiring higher doses in variable-dose studies.³

Posttreatment Care

No specific interventions are required after injection of BoNTA-ABO. Gentle pressure can help reduce ecchymosis and oozing from the skin puncture sites. Ice packs placed for five to 10 minutes may help reduce discomfort and swelling after injection. As with BoNTA-ONA, controversy exists regarding posttreatment activity. We caution against heavy exercise or straining for three to four hours posttreatment.

Combination Treatments

BoNTA-ABO can be combined with other treatments, such as dermal fillers. The use of dermal fillers is indicated for static rhytids or dermal atrophy that would not be affected by paralysis of the underlying muscle. This is most common in static vertical glabellar creases. Injections can be performed at the same time or delayed two weeks. The latter allows the toxin to take full effect, to determine the actual need for a dermal filler.

Many other combinations with resurfacing and injectable fillers are feasible. For example, BoNTA-ABO can be injected into the lateral orbicularis oculi muscle in conjunction with lower lid laser resurfacing and dermal fillers to the lower crow's feet to avoid paralysis of the zygomaticus major muscle. BoNTA-ABO can also be injected into the orbicularis oris muscle in conjunction with fillers to the lip and laser resurfacing of the vertical lip lines. If the patient is new to botulinum toxin use and the full clinical response is unclear, it may be best to administer filler conservatively or wait until a later appointment to avoid overcorrection. One must also keep in mind that many dermal fillers last six months to one year, so repeat filler treatments may not be necessary with every subsequent BoNTA-ABO treatment.

Common Adverse Effects

The most common adverse effects are injection site discomfort, fatigue, injection site pain, muscle weakness and musculoskeletal pain, dysphagia and dry mouth, headache, infection, dysphonia, and eyelid disorders. These occurred in patients receiving up to 1000 units of BoNTA-ABO for the treatment of cervical dystonia.¹ Of note, the typical doses of BoNTA-ABO for cosmetic uses are much less than 500 units (Table 1). Clinically, the most common adverse effect is punctuate bruising and injection site pain, both of which can be minimized with experience, but which also will inevitably happen regardless of precautions taken.

Typically, as with any neurotoxin, care must also be taken when injecting approximately one fingerbreadth above the lateral eyebrow. Completely ameliorating rhytids in this region will result in inability of the patient to raise their eyebrow. Subsequently, iatrogenic dermatochalasis can occur from overzealous or improper injection in the temporal region leading to brow ptosis. In addition, upper eyelid ptosis is theoretically possible from diffusion or spread of the toxin into the levator palpebrae superioris muscle of the eyelid. Targeting injections at least 1 cm above

the bony superior orbital rim, injecting lower volumes to reduce toxin spread, and using lower doses to reduce toxin diffusion can theoretically minimize this complication.

SUMMARY OF STEPS

The administration of BoNTA-ABO should be performed as follows:

- Pretreatment preparation includes patient evaluation, patient education, informed consent, and posttreatment photographs.
- Toxin requires refrigeration at 2°C to 8°C (36°F–46°F) and protection from light until it is used.
- Reconstitution with 2.5 mL of preservative-free sterile saline leads to 10 units per 0.8 mL; reconstitution with 1.5 mL of saline leads to 10 units per 0.5 mL.
- Typical dosages for BoNTA-ABO differ significantly from BoNTA-ONA and should be adjusted for type of toxin used, the anatomic region treated, muscle bulk, and previous patient response.

CONCLUSIONS

Neurotoxins as an aesthetic treatment have dramatically exceeded any initial expectations and have far-reaching consequences. BoNTA-ABO is an established derivative of botulinum toxin that has a long history of safe use outside of the United States for both aesthetic and nonaesthetic indications. Since its FDA approval in 2009 for the treatment of glabellar lines and cervical dystonia, we have incorporated BoNTA-ABO use into our aesthetic practice. Previously, BoNTA-ONA was the only botulinum toxin A derivative approved for aesthetic use in the United States, and we have enjoyed extensive experience with its use and continually growing applications. Experience with BoNTA-ABO is limited and evolving. In addition to the learning curve for mentally adjusting unit dosing between BoNTA-ABO and BoNTA-ONA, there is still knowledge to gain in practical application, clinical response, and patient acceptance. As further clinical experience is acquired, one should feel comfortable with the use of BoNTA-ABO and achieve the same safe and predictable results that are enjoyed with other botulinum toxins for aesthetic applications. Despite the learning curve for dosing, the fundamental concepts, injection techniques, and targeted anatomy remain the same. This guide is intended to serve as a starting point for those incorporating BoNTA-ABO into their practice. ■

DISCLOSURES

The authors have no disclosures with respect to the content of this article.

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