

# Botulinum toxin type A for aging face and aesthetic uses

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**ABSTRACT:** Botulinum neurotoxin type A injection to correct and/or reverse the physical effects of aging process has become one of the most frequently requested cosmetic procedures at an outpatient setting. Careful clinical evaluation together with proper use of the techniques, including pre- and post-procedures recommendations, reconstitution of the products, techniques, and doses, are described in this article. This article also covers the main indications of botulinum neurotoxin type A for aging face and other aesthetic uses, as well as some possible adverse reactions and their management.

**KEYWORDS:** aesthetic procedures, aging face, botulinum toxin, clinical practice, rejuvenation

## Introduction

Botulinum neurotoxin type A (BoNTA) injection (1,2) is a simple, safe, and very effective treatment of the aging face, reducing wrinkles through the transitory and reversible paralysis of treated muscles. It can be combined with other invasive and/or minimally invasive procedures such as fillers and lasers, to improve the cosmetic results (3).

Since its approval for cosmetic use by the Food and Drug Administration, many studies and reviews have been published showing safety and efficacy of BoNTA injections (2,4–8). The establishment of more accurate and standard doses for each indication as well as number and location of the injection sites has also been the aim of some publications (9–11).

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## Pre- and post-procedure recommendations

Discussing patients' expectations and requests previous to treatment is crucial to provide realistic expectations regarding the treatment results. Effects and potential side effects should be also mentioned to the patients. For a more detailed evaluation of the treatment outcomes, photographs should be taken at rest and contracting the target muscles before the procedure (12).

Makeup should be removed, and antisepsis of the skin is carried out using 70% isopropylalcohol or iodine (3). Care should be taken to minimize undesired side effects and to increase patients' comfort. Pain at the injected sites can be reduced by applying topical anesthetics, and cold air or iced compresses or devices before each injection (3,13). Weiss and Lavin reported vapocoolants as safe and effective to reduce discomfort and anxiety during BoNTA injections in the glabellar area (14).

Common post-procedure recommendations are: Patients must remain in the vertical position, and avoid intense physical exercise and manipulating the injected area for at least 4 hours after injections. These measures may prevent the action

of BoNTA in the adjacent muscles, which are not desirable (15).

## Technique

Aiming to reach the most effective and long-lasting results, some precautions concerning the storage and reconstitution of BoNTA are advisable.

Manufacturers recommend that reconstitution be done few hours prior to use with 0.9% sterile saline solution. Nonetheless, some studies showed that BOTOX® (Allergan Inc., Irvine, CA, USA) and DYSPORT® (Ipsen Ltd., Maidenhead, UK) remain safe and effective from 2 to 6 weeks, respectively, after reconstitution (16–18). When preservatives are added, it is suggested that the storage period may be long, because they reduce the risk of bacterial contamination (3).

One to 10 mL is used for dilutions, considering cosmetic purposes (Table 1), but low volumes are preferred, as they result in higher concentration of the product, leading to a more precise injection technique and decreasing the risk of complications. Bubble formation has to be avoided when reconstituting the product (3).

The dose equivalence between BOTOX® and DYSPORT® has been studied but is still matter of debate. It has been suggested that dose ratios of less than 1 : 3 U between these two formulations are more suitable (19), and based on recent studies carried out in humans, the ratio seems to be 1 : 2.5 U or lower (20). A study showed that the dose equivalence of 1 : 2.5 U (between BOTOX® and DYSPORT®) produces similar results regarding

action halos of muscular and sweat gland activity (21). Other studies also showed that the dose equivalences of 1 : 2 to 1 : 2.5 (between BOTOX® and DYSPORT®) have similar results regarding efficacy, intensity, and duration of the paralysis or anhydrosis, and safety (Table 1) (22–24). According to Karsai and Raulin, the dose equivalence of 1 : 2.5 U between BOTOX® and DYSPORT® is adequate (25).

BoNTA injections are usually performed on an outpatient basis with the patient seated in a chair with a raised head support (3). Physicians must evaluate the patient, analyzing the facial anatomy, observing patients at rest and contracting their muscles, and paying attention for any preexisting asymmetry (10). The injection sites are selected according to the previous assessment and are marked with a skin-marking pen. Injections must be symmetrical not only in relation to the sites, but also to the doses applied, except when patients show any asymmetries (3). Injections must be superficial (3) and are usually performed with small syringes and fine-gauge needles (FIG. 1).

A study performed with 37 patients evaluated if there was a preference for 30-gauge needle or for 32-gauge needle in the patient's opinion. The results showed no statistically significant differences between these two needles regarding the amount of intra-procedural pain ( $p = 0.37$ ) or the level of post-procedural pain and discomfort ( $p = 0.76$ ) experienced by patients (26). In case of hematomas, cold compress or soft manual compression is applied directly to the spot where the vessel was punctured (3).

**Table 1.** Volumes of 1, 2, and 2.5 mL used to reconstitute BOTOX® 100 U per vial and the recommended equivalent doses and volumes to reconstitute DYSPORT® 300 and 500 U per vial, and AZZALURE® (Ipsen Ltd., Maidenhead, UK) 125 U per vial at the equivalent doses of 1 : 2, 1 : 2.5 U and 1 : 3. (3)

To achieve the equivalence between BOTOX® and DYSPORT®/AZZALURE® of (U)	If the vial of 100 U (BOTOX®) is usually diluted in (mL)	The vial of 500 U of DYSPORT® should be diluted in (mL)	The vial of 300 U of DYSPORT® should be diluted in (mL)	The vial of 125 U of AZZALURE® should be diluted in (mL)
1 : 2	1	2.5	1.5	0.625
	2	5	3	1.25
	2.5	6.25	3.75	1.562
1 : 2.5	1	2	1.2	0.5
	2	4	2.4	1
	2.5	5	3	1.25
1 : 3	1	1.66	1	0.41
	2	3.2	2	0.83
	2.5	4.08	2.5	1.04



FIG. 1. Small syringes are recommended for botulinum neurotoxin type A injections.



FIG. 2. Pinching the corrugator muscle and proper position of the syringe make the botulinum neurotoxin type A injections safer and more comfortable.

## Upper face applications

### Glabella

Treatment of the glabellar region remains the most common indication for BoNTA, targeting the *procerus* muscle (m.) and *corrugator supercilii* (m.).

The same glabellar injection points are used for all BoNTA products, usually three to five points (27).

BoNTA is slowly injected into the belly of the *corrugator* m., keeping the needle tip at a distance of approximately 1 cm superior to the orbital rim (3). The position of the needle is perpendicular and slightly advanced within the muscle fibers in a vertical direction toward the hairline (FIG. 2) (28).

One or two points can be applied into the belly of the *procerus* m. to treat the horizontal lines at the root of the nose. This muscle is treated in the midpoint of an imaginary "X" formed by lines

joining the inner brows and the contralateral inner canthus (3). The medial aspect of the eyebrow is considered in the conventional injection technique. In patients with a long *procerus* m., the dose can be injected in two points of this muscle. If the *frontalis* m. is not treated, the middle to lateral portion of the eyebrows will be slightly raised by the opposing levator action of the *frontalis* m. (28,29). To avoid the elevation of the middle to lateral portion of the brow, the injection is done at the midpoint of the eyebrow, at least 1 cm above the supraorbital prominence (28).

The eyebrow is elevated by the *frontalis* m. and depressed by the medial brow depressors, *corrugator supercilii* m. and *procerus* m., and the lateral brow depressors, lateral portion of *orbicularis oculi* m. (30). The paralysis of these muscles allows for unopposed brow abduction by the *frontalis* m. BoNTA treatment for glabellar lines causes an elevation of the medial eyebrow, which produces a pleasant aspect of the brow.

Doses are referred in Table 2. Men generally require higher doses of BoNTA than females because bigger muscles require a higher dose to achieve a similar effect (10).

Eyelid ptosis is the most feared complication related to BoNTA injections on the glabellar area. To prevent this transitory effect, it is important to avoid direct injection at the levator palpebrae superioris, to avoid massaging at the injected area, or injecting larger amounts of BoNTA. Other common injection-related side effects in the glabellar area are headache, injection site pain, transitory edema and erythema or bruising, and nasopharyngitis (2).

### Periorbital area

Periorbital rhytides or crow's feet wrinkles are radial lines mainly caused by the hyperactivity of the orbital portion of the *orbicularis oculi* m. (3).

Injections are performed at dermis typically placed 1 cm lateral to the orbital rim at three sites overlying the lateral fibers of the *orbicularis oculi* m., avoiding injecting the *zygomaticus* m. (5). In order to prevent accidents, the needle must be always oriented away from the orbit of the eye, and the injections should preferably be performed in the superficial dermis, avoiding or minimizing bleeding (FIG. 1) (31). The needle should be parallel to the skin, avoiding touching the periosteum. The number of injection sites is usually two to five. Table 2 presents suggested doses for this area, but it should be customized according to the patient's needs.

**Table 2.** Suggested total doses of DYSPORT® and BOTOX® based on the consensus groups for DYSPORT® and BOTOX®, and other publications (3,9–11)

Indications	Total doses of DYSPORT® <sup>a</sup> U	Total doses of BOTOX® <sup>a</sup> U
Glabella	30–70	10–40
Periorbital area	30–60	10–30
Forehead	20–60	6–15
Lower eyelid wrinkles	5	2
Bunny lines	10–20	4–8
Nasal tip	5–10	2–3
Repeated nasal flare	10–20	4–10
Marionette lines	10–20	3–6
Perioral wrinkles	4–12	4–5
Dimple chin	10–20	4–10
Gingival smile	5–15	2–4
Platysmal bands	Maximum of 50 per side	40–60 total per neck
Décolleté wrinkles	75–120	30–100

<sup>a</sup>Muscle anatomy and each case should be particularly considered because of common differences among individuals.

To avoid the worsening of skin laxity and eye bags, the treatment is contraindicated to patients with laxity of the canthal tendon and/or with retraction of the lower eyelid. It is also contraindicated when the wrinkles are due to the action of the *zygomaticus major* m. or when patients have been submitted to ablation resurfacing or blepharoplasty of the lower eyelid, without canthopexy (9,31).

Complications related to this area include bruising, diplopia, ectropion or a drooping lateral lower eyelid, and asymmetric smile because of the injection in the *zygomaticus major* m. (32). To avoid these, it is important to place injections at least 1 cm outside the bony orbit or 1.5 cm lateral to the lateral canthus, and to avoid injections medially to vertical line through the lateral canthus neither close to the inferior margin of the zygoma (32).

### Forehead

The *frontalis* m. is an elevator muscle that lifts the forehead and eyebrows, and is responsible for producing transverse forehead wrinkles. The benefit of the treatment of these muscles should be carefully evaluated, and for some patients, the treatment of the upper part of these muscles is the best option, because the treatment of the entire frontal region causes significant loss of facial expression (masked appearance). Moreover, total paralysis of the *frontalis* m. can cause brow ptosis (28). The frontal region should always be treated in association with the glabellar area for more satisfactory results, avoiding the excessive use of glabella's muscles, which are mainly depressors (33,34). Five to 10 points are usually injected in the forehead,



**FIG. 3.** Treatment of the forehead with botulinum neurotoxin type A injections.

depending on the extent of the area to be treated, whether totally or partially. Points' distribution should be established through physical examination of each patient and is generally horizontal or V-shaped (3). Table 2 presents suggested doses for the forehead area (FIG. 3).

Special techniques are required to compensate asymmetries. It is important that all injections are performed from 1 to 2 cm above the orbital border in order to reduce the risk of eyebrow *ptosis* that can provide a tired look to the patient.

### Midface

#### Lower eyelid wrinkles

Lower eyelid wrinkles are usually the result of hyperkinetic activity of this part of the *orbicularis*



**FIG. 4.** Lower doses are delivered in superficial injections for the treatment of lower eyelid wrinkles.

*oculi* m. BoNTA injections attenuate these wrinkles and, also, may increase the palpebral aperture. Although effective in diminishing the hyperkinetic lines, it is not recommended to treat the static wrinkles caused by photodamage or other causes, such as skin laxity (11). In these cases, combination therapy would be recommended.

Lower eyelid wrinkles should be treated together with the lateral periorbital wrinkles to achieve better results. For this indication, lower doses and superficial injections should be used (FIG. 4). The treatment of lower eyelid with BoNTA in individuals with lower eyelid laxity or recent lower blepharoplasty should be avoided (35,36). Doses are referred in Table 2 and should be divided in one or two injection sites.

### Bunny lines

Nasal wrinkles, called “bunny lines,” refer to the wrinkles on the lateral part of the nose, which result from the contraction of the transverse portion of the *nasalis* m. Usually, they are dynamic wrinkles and appear when patients laugh or frown (11). Furthermore, they may become more pronounced after glabellar and periorbital BoNTA treatment (35).

Lower doses are used in the transversal areas of the nasal bone (36). The injection must be applied in the high lateral nasal wall, below the angular vein (FIG. 5). In order to avoid ptosis of the upper lip, injections should not be applied near to the nasofacial groove (35,37). Suggested doses for this area are present in Table 2.

The treatment may be less effective in patients who recruit these muscles excessively or have had prior rhinoplasty (35).



**FIG. 5.** Bunny lines are treated by one injection in each side of the dorsum of the nose, to reach the *nasalis* m.

### Nasal tip

The *depressor septi nasi* m. is a small muscle located in the external inferior base of the nasal septum. Its contraction contributes to the nasal tip lowering, aggravating the nasal tip ptosis that usually occurs with aging. Perpendicular injection is recommended in a single site just below the nose tip in the columella and can produce a slight lift of the tip of the nose (9). The usual total doses are referred in Table 2.

### Repeated nasal flare

Some people present dilated or rhythmic contractions of the nostrils on certain occasions. Injections of BoNTA are indicated on each side in the lower nasal fibers above the lateral nasal ala to treat this condition (35). Doses are referred in Table 2.

## Lower face applications

### Marionette lines

The *depressor anguli oris* m. contributes to droop the mouth corners, giving a sad expression to the face (11,35). BoNTA can be used to weaken this muscle, elevating the mouth corners or returning them to a neutral position (35). Injections should be done bilaterally, in a point above the mandibular angle in an imaginary line that follows the direction of the nasolabial groove (3). Visualization of the muscle can be obtained by asking the patient to grind his/her teeth or to grimace (11). The suggested doses are referred in Table 2.



**FIG. 6.** Small doses of botulinum neurotoxin type A can be delivered in one or two sites in each side of the upper lip.

### Perioral wrinkles

The lips and the perioral region have an important role in the aesthetic balance of the face. The treatment of perioral wrinkles are usually done with fillers (11,38). Perioral wrinkles are caused by the contraction of *orbicularis oris* m. associated with photodamage, intrinsic aging, and hereditary factors (3).

Small doses of BoNTA produce localized slight paralysis of the *orbicularis oris* m., reducing perioral lines and slightly improving the appearance of the lips (35). Injections points should be done at the vermillion border, parallel to the lips and at least 1.5 cm away from the mouth corners (11). The total dose should be distributed in four to six points, being four at the upper lip and two at the lower lip (FIG. 6). Low doses and superficial injections are preferred to avoid functional impairment of the lips (11,39). The doses are referred in Table 2.

The treatment of the perioral area may be optimized by using combined procedures with BoNTA, such as fillers and lasers (39).

### Dimpled or “cellulitic” chin (“peau d’orange”)

The contraction of *mentalis* m. associated with loss of collagen and subcutaneous fat produces the dimpled aspect of the chin (35,39). Treatment with BoNTA can be used to restore a smooth appearance of the chin (11).

Usually, two injection points at the prominence of the chin result in a cosmetically appropriate outcome (11). In order to prevent mouth asymmetry or lower lip ptosis, the injections should be done close to the mandibular bone (FIG. 7).

The contraction of *mentalis* m. can also promote lower lip projection. Thus, when dimpled chin and



**FIG. 7.** Treatment of the *mentalis* m. with botulinum neurotoxin type A injections is done in two points close to the mandibular bone.



**FIG. 8.** Treatment of the platysmal bands or décolleté wrinkles.

drooping mouth corners are treated together, lower doses per point are recommended in order to prevent the overtreatment of this condition (11).

The recommended doses as referred in Table 2.

### Gingival smile

Gingival or “gummy” smile is an anatomic variant of smile in which there is an excessive gingival exposure, usually more than 2 mm, sometimes associated with aesthetic embarrassment. It is mainly caused by the contraction of the *levator labii superioris* m. (40).

Injections should be done at one point on each side of nasolabial groove into the *levator labii superioris alaeque nasi* m., about 5 mm from the nasal ala rim (40,41). Table 2 presents suggested doses for gingival smile.

## Asymmetric smile

Asymmetric smile can be the result of hyperkinesis of the *depressor labii inferioris* m. or a segmental weakness of the *levator labii superioris* m. (3,8). Injections of BoNTA are a simple, noninvasive, and safe way to correct asymmetric smile (8). The number of points and total doses are defined individually according to the muscle involved.

Results become evident in less than 5 days, and the effects last from 4 to 5 months after the first treatment. In subsequent treatments, it is recommended to reduce the doses, and the results last usually longer (8).

## Platysmal bands

The *platysma* is a thin muscle that extends from the border of the lower jaw to the clavicular region (11). Its contraction may result in horizontal wrinkles and vertical bands, not only in the cervical region, but also in the *décolleté* area (42). Although most of neck wrinkles are related to photoaging and skin laxity, BoNTA can be an efficient and safe treatment to neck aging (11). It acts by producing a partial paralysis of the anterior part of the *platysma* m., softening the vertical platysmal bands (35). Ideal patients for this indication should have a thin and good skin elasticity, and little or no fat or sagging skin (11). BoNTA should be applied on the *platysma* band with superficial intramuscular injections (FIG. 8). Potential adverse effects such as dysphasia, dysphonia, and neck weakness can be minimized by using the correct technique and doses (11), following the consensus recommendations, as referred in Table 2.

## Décolleté

Anterior mid-chest wrinkles result from extrinsic and intrinsic factors, such as the position adopted during sleep, photodamage, and action of medial fibers of *pectoralis major* m. and the tail portion of the *platysma* m. (11,43).

BoNTA can be used when clinical exam shows the involvement of the mentioned muscles. Four to six injection points can be applied in each side, in a “V” shape, plus the treatment of caudal part of *platysma* m. The total dose is referred in Table 2.

## Conclusion

BoNTA has been used in the last 20 years in medical and cosmetic dermatology for the treat-

ment of facial wrinkles and has become one of the most popular cosmetic procedures. It is a quick and very effective treatment with fast or immediate recovery, and leads to a high degree of patient satisfaction.

A great number of published studies have demonstrated BoNTA to be a safe, predictable, and very effective treatment for a number of cosmetic indications, being approved in many countries by the respective regulatory agencies.

The keys to success in the cosmetic use of BoNTA are knowledge of anatomy, physiology, action mechanism, appropriate technique and doses, and, also, potentials and possible complications.

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