

Global Aesthetics Consensus: Botulinum Toxin Type A—Evidence-Based Review, Emerging Concepts, and Consensus Recommendations for Aesthetic Use, Including Updates on Complications

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Background: Botulinum toxin type A injection remains the leading nonsurgical cosmetic procedure worldwide, with a high rate of efficacy and patient satisfaction.

Methods: A multinational, multidisciplinary group of plastic surgeons and dermatologists convened the Global Aesthetics Consensus Group to develop updated consensus recommendations with a worldwide perspective for botulinum toxin and hyaluronic acid fillers. This publication on botulinum toxin type A considers advances in facial analysis, injection techniques, and avoidance and management of complications.

Results: Use of botulinum toxin has evolved from the upper face to also encompass the lower face, neck, and midface. The Global Aesthetics Consensus Group emphasizes an integrative, diagnostic approach. Injection dosage and placement are based on analysis of target muscles in the context of adjacent ones and associated soft and hard tissues. The indication for selection of botulinum toxin as a primary intervention is that excessive muscular contraction is the primary etiology of the facial disharmony to be addressed. Global Aesthetics Consensus Group recommendations demonstrate a paradigm shift toward neuromodulation rather than paralysis, including lower dosing of the upper face, more frequent combination treatment with hyaluronic acid fillers, and intracutaneous injection where indicated to limit depth and degree of action.

Conclusions: The accumulation of clinical evidence and experience with botulinum toxin has led to refinements in treatment planning and implementation. The Global Aesthetics Consensus Group advocates an etiology-driven, patient-tailored approach, to enable achievement of optimal efficacy and safety in patient populations that are rapidly diversifying with respect to ethnicity, gender, and age. (*Plast. Reconstr. Surg.* 137: 518e, 2016.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, V.

Botulinum toxin type A injection is the most common cosmetic procedure globally. Surveys from core aesthetic specialty organizations consistently rank it first on lists of member-reported, nonsurgical aesthetic procedures. In 2014, the American Society for Aesthetic Plastic Surgery reported more than

3.5 million botulinum toxin procedures.¹ The International Society of Aesthetic Plastic Surgery survey reported more than 4.8 million procedures worldwide in 2014,² and the 2013 American Society for Dermatologic Surgery survey found a 20 percent increase compared with 2012.³ Similar trends are reported in Europe⁴ and Asia.

Aesthetic use of botulinum toxin type A is supported by a broad literature base. Of the available formulations, onabotulinumtoxinA (Allergan, Inc., Irvine, Calif.) has the most approved clinical indications. It is the most widely studied formulation for cosmetic and therapeutic purposes,

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The faculty of the Global Aesthetics Consensus Group is listed in the Appendix.

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with more than 2800 clinical and nonclinical articles published between 1986 and 2013, and more than 400 peer-reviewed articles.⁵ The body of literature that addresses abobotulinumtoxinA (Galderma Laboratories, L.P., Fort Worth, Texas), incobotulinumtoxinA (Merz Pharmaceuticals, Raleigh, N.C.) and other formulations is also growing.

North American consensus recommendations for botulinum toxin type A were revised and updated in 2008.⁶ European (French) guidelines were published in 2011.^{7,8} Comparative guidelines for onabotulinumtoxinA, abobotulinumtoxinA, and incobotulinumtoxinA were provided by five experts from Canada, Europe, and South America in 2013.⁹ Treatment strategies have progressed rapidly, reflecting increasing patient diversity with respect to gender, age, and ethnicity, as well as the growing number of patients who receive repeated treatment over years or decades. Geographic variations have evolved as worldwide use has expanded. This is a manifestation of prevalent facial morphotypes and global migration patterns, and also of cultural differences in aesthetic ideals. The 2014 American Society for Aesthetic Plastic Surgery survey results exemplify these demographic trends, reporting that approximately 22 percent of all cosmetic procedures were performed on ethnic minorities, and approximately 11.5 percent of botulinum toxin procedures were performed on men.¹

CONSENSUS OBJECTIVES AND METHODOLOGY

In January of 2014, a multinational group of key opinion leaders in plastic surgery, dermatology, facial plastic surgery, and oculoplastic surgery convened the Global Aesthetics Consensus Group. The objectives were to review aesthetic applications of botulinum toxin type A and

Institut Biochimique SA, Kythera, Merz, and Teoxane. Arthur Swift, M.D., states that he is a speaker, clinical researcher and advisor to Allergan, Galderma, and Merz. Ada R. Trindade de Almeida, M.D., states that she is an advisor for Allergan, Merz, Galderma, Roc, and Mantecorp, has participated in clinical trials for Allergan, and is a speaker for Allergan and Theraskin. Yan Wu, M.D., states that she serves as a consultant and/or clinical investigator for Allergan, GlaxoSmithKline, Lanzhou Biological Products Institute, and Freda Biopharm (Shandong hyaluronic acid filler).

Table 1. Methodology for Global Aesthetics Consensus Group Panel Consensus

Grading of Statements and Opinions Developed during the Conference*†	
Grade A	Recommended
Grade B	Reasonable choice
Grade C	Not fully established (unclear risk/benefit, inadequate data)
Grade D	Not recommended

Consensus was defined as $\geq 66\%$ of polled panel members selecting a consensus grade (e.g., 11 of 16 polled panel members).
 Minimum number of polled panel members allowed was 11.
 If no statement/opinion grade reached the two-thirds level, results were reported as “no consensus reached.”
 Plurality or majority selection of consensus grade may be reported.

*Select results of premeeting treatment survey are included where instructive. †For purposes of discussion, the consensus recommendations divide the face into thirds (upper, middle, and lower). However, the panel stressed the importance of an integrative approach to both assessment and treatment.

hyaluronic acid fillers, and to provide updated consensus recommendations. The methodology used by the panel for determining consensus is summarized in Table 1. This publication presents the panel’s recommendations and position statements for botulinum toxin, based on integration of its clinical experience with published data. It includes new guidelines for treatment planning and implementation, and updates to previous guidelines for avoidance and management of complications from aesthetic use of botulinum toxin. Another publication in the Global Aesthetics Consensus Group series provides recommendations for combined treatment with botulinum toxin and hyaluronic acid fillers, and optimization of treatment outcomes in diverse patient populations.¹⁰

BOTULINUM TOXIN TYPE A: INDICATIONS AND PRACTICAL CONSIDERATIONS

Since 2009, the U.S. Food and Drug Administration has mandated nonproprietary names for botulinum toxin type A formulations that it approves for aesthetic or therapeutic use.¹¹ This is to clarify that different formulations are chemically and pharmacologically unique, that their doses are not interchangeable, and that their dose-response curves are not parallel.^{11–15}

OnabotulinumtoxinA has regulatory approval under brand names that include Botox Cosmetic, Vistabel, Vistabex, and Botox Vista. AbobotulinumtoxinA has approval under the brand names Dysport and Azzalure, and incobotulinumtoxinA has approval under the brand names Xeomin, Xeomeen, and Bocouture. The formulations are approved in numerous countries for treatment of glabellar lines. Additional indications in some countries include treatment of lateral canthal lines, facial hyperkinetic lines, and/or upper facial lines.⁵ Off-label use for other aesthetic indications is common.

Table 2 summarizes Food and Drug Administration product labeling for reconstitution, storage, and administration of onabotulinumtoxinA, as well as off-label methods used by the panelists.¹² A postapproval double-blind, randomized, controlled study demonstrated less procedural pain after reconstitution with benzoic acid-preserved (bacteriostatic) 0.9% saline.¹⁶ A recent expert consensus concluded unanimously that reconstituted botulinum toxin can be refrigerated or refrozen for at least 4 weeks before injection without significant risk for contamination or decreased effectiveness, and used to treat multiple patients, assuming

Table 2. U.S. Food and Drug Administration Product Labeling for Reconstitution, Storage, and Administration of OnabotulinumtoxinA and Off-Label Methods Used by Consensus Panelists

Parameter	Recommendation
Diluent	FDA labeling: nonpreserved 0.9% saline ¹² with appropriate storage and safety measures Panelists’ preference: preserved (bacteriostatic) 0.9% saline*
Concentration and dosing	FDA labeling: 4 U/0.1 ml with a total treatment dose of 20 U in 0.5 ml for glabellar lines and 24 U in 0.6 ml for lateral canthal lines ¹² Panelists’ preference: a range of concentrations (e.g., from 2 to 10 U/ml) may be appropriate to deliver the required dose per injection site*
Storage	
Before reconstitution	FDA labeling: 2°C to 8°C for up to 24 months ¹²
After reconstitution	FDA labeling: storage at 2°C to 8°C and administration within 24 hours ¹² Panelists’ preference: storage in stoppered vial or as aliquots drawn from vial into sterile syringes, for 4 to 6 weeks at 4°C ^{17–20*} Freezing after reconstitution may also be appropriate ¹⁷

FDA, U.S. Food and Drug Administration; *U.S. Food and Drug Administration off-labeling. Volume per unit dose is inversely proportional to reconstitution volume. Lower volume per unit dose may limit postinjection spread; the decreased volume to deliver the required dose may decrease injection pain. Higher volume per unit dose may increase postinjection spread.

Table 3. Summary of Prospective Simulation Study of Sterility of Multiple-Use Botulinum Toxin Type A Vials*

Methods
—Consecutive 100-U vials of onabotulinumtoxinA were each reconstituted with 2.5 ml of 0.9% saline with preservative (benzoic acid)
—Within 1 week of reconstitution, each vial was used to treat 1 to 3 patients. A total of 60 to 80 U was withdrawn from each vial.
—Vials were stored in a plastic kidney basin in an unlocked, multiple-use refrigerator for medications.
—After 2 weeks of refrigeration, a randomly assigned nurse withdrew and discarded 0.1 ml from each vial using the same technique as for therapeutic use.
—Cycles of withdrawal and discarding were continued until a 0.1-ml aliquot could not be withdrawn without prying off the metal cover of the vial.
—Vials were then sent to a microbiology laboratory for sterility testing using thioglycollate broth medium.
Results
—127 vials were handled per protocol.
—Each vial underwent a mean of 4.5 access procedures, including 1.6 therapeutic extractions. A total of 76 U was removed during a period of 7 weeks.
—Sterility analysis with thioglycollate broth indicated no evidence of contamination.

*Adapted from Alam M, Yoo SS, Wrone DA, White LE, Kim JY. Sterility assessment of multiple use botulinum A exotoxin vials: A prospective simulation. *J Am Acad Dermatol.* 2006;55:272–275.

there is appropriate handling.¹⁷ This affirms previous postapproval data^{18,19} and a prospective simulation study of common, off-label reconstitution and storage methods (Table 3).²⁰ Some panelists prefer higher reconstitution volumes and, hence, injection volumes per unit dose, when they desire greater toxin spread. Others feel that higher volumes are associated with more procedural pain and greater temporary postprocedural visibility of injection sites.

EVOLVING PARADIGMS IN PATIENT ASSESSMENT AND TREATMENT PLANNING

Panfacial, Diagnostic Approach

Although the face is discussed in horizontal one-thirds in this consensus document, the panel stressed the importance of an integrated, panfacial approach. The original paradigm with toxin and fillers was to relax the upper face, fill the midface, and relax and fill the lower face.⁶ Appropriate patient assessment and understanding of the etiology of what is observed catalyze an evolution toward more equal use of toxin and fillers in all facial zones. Muscles are targeted where their excessive contraction is the primary cause of the changes that are seen. Volume is restored where this is the primary cause.

Full assessment for botulinum toxin treatment includes anatomical and functional analysis of the musculature in the context of facial morphology and the qualitative and quantitative status of hard and soft tissues. Full understanding of the relationships between muscles is

required. Skin snap and stretch tests are valuable for revealing soft-tissue quality and the etiology of rhytides. When determining whether botulinum toxin is appropriate, the risk of impaired function must be considered. This diagnostic approach allows selection of the safest and most effective treatment option with modification for repeated treatments, older patients, and the emerging indication of early, proactive, or even preventive treatment of younger patients. Treatment planning in these situations is discussed in the Global Aesthetics Consensus Group publication on combined treatments and optimization of outcomes in diverse patient populations.¹⁰

Patient-Tailored Approach

It is crucial to establish good physician-patient rapport, assess patients' objectives^{21,22} in the context of what is seen on examination, and provide patient education. Verbal education can be supplemented by written handouts, visual aids, audiovisual media, and content from Internet websites.

Although the original objective of botulinum toxin treatment was to paralyze target muscles, current understanding is that the most desirable outcome is modulation of muscular activity. The consensus panel noted trends in daily practice toward decreased dosages and increased injection intervals. This is supported by a recent retrospective medical chart review of 194 patients who received onabotulinumtoxinA to treat glabellar lines during a mean of 9.1 years.²³ Separate analysis of the same data set demonstrated sustained patient and physician satisfaction with repeated treatment.²⁴ Patients reported greater reduction

in their perceived age as they received treatments for longer periods.²³

While it is useful to recognize the influence of demographic characteristics such as gender or ethnicity on rhytide patterns,^{25–29} the key to successful treatment is individualized patient assessment. Cultural expectations are not synonymous with ethnic origin, and patients may have specific preferences regarding the magnitude and nature of results. Validated wrinkle classification and rating scales^{30,31} and software programs that depict age-related changes³² can be of value in communicating expected outcomes to patients.

Comprehensive facial assessment encompasses both static and dynamic observation. The real image of a patient, and thus, the most accurate pretreatment evaluation, is obtained through observation of spontaneous animation rather than animation on command. Therefore, assessment begins before formal examination, during history-taking and while the physician and patient are in dialogue. In a panfacial context, individual muscle mass, anatomy, and contraction pattern can guide appropriate toxin dosing and placement.^{33–36} It is helpful to use validated grading scales for muscle mass³³ and to palpate muscles while visualizing them.³³

Approach to Multiple Areas

The indications for treating a facial area are the same, whether single or multiple areas are to be addressed. Aging occurs as a continuum across areas. The panel observed that treatment of two adjacent areas can produce the same or potentially better results with reduced dosage per injection point. Conversely, overcorrection of one area may cause local improvement, but it will usually cause detriment to the surroundings, through unnatural appearance and/or recruitment of other muscles that were previously less active.

Given the trend toward lower dosing, clinicians should be mindful of the balance between efficacy and aesthetic outcome. The quality of results should not be subordinated to their longevity. Repeated, high dosing of some muscles may cause atrophy and, hence, volume loss. The possibility of compensatory hypertrophy in non-target muscles should also be considered (e.g., hypertrophy of temporalis and/or pterygoid muscles when targeting the masseter).

Prospective, randomized, placebo-controlled studies show that treatment of multiple upper facial lines with onabotulinumtoxinA

significantly improves patient-reported outcomes. One study involved 40 subjects.³⁷ Another, which involved 917 subjects, investigated treatment of lateral canthal lines alone (12 units per side) or together with glabellar lines (20 units).³⁸ Investigator and patient assessments revealed greater benefit when lateral canthal and glabellar lines were treated simultaneously. An additional trial of 445 subjects evaluated onabotulinumtoxinA in treatment of lateral canthal lines alone and led to approval by the European Union and U.S. Food and Drug Administration for this indication.³⁹

Younger and Older Patients

A comprehensive review of emerging concepts in facial aging and how patient age impacts treatment is provided in the Global Aesthetics Consensus Group publication on combined treatments and optimization of outcomes in diverse patient populations.¹⁰ The objective to prevent rhytides is most applicable to younger patients. Loss of volume and consequent deflation of the soft tissues and underlying, supportive bone are cardinal features of facial aging.^{40–46} The majority of the consensus panel considered it critical to development of age-appropriate treatment goals to understand that these changes may impact muscular activity as well as facial contours. A greater proportion of rhytides in older patients may be due to loss of skin elasticity. They can be ameliorated by multiple modalities, including botulinum toxin, but probably not toxin alone. Lower doses may be appropriate, due to changes in muscle mass and function with age.

CONSENSUS RECOMMENDATIONS

Consensus recommendations for onabotulinumtoxinA injection sites and dosages are provided in Tables 4 through 6. Table 7 provides general Global Aesthetics Consensus Group recommendations and position statements. The recommendations may be extrapolated with care, and appropriate dosages, to other botulinum toxin formulations.

Upper Face: Glabellar, Lateral Canthal, and Horizontal Forehead Lines

Premeeting panel surveys indicated that botulinum toxin alone was the most common approach for the upper face (Fig. 1). Growing evidence supports treatment of the glabella and lateral canthal lines, or of multiple areas including

Table 4. Consensus Recommendations and Expert Panel Opinions Regarding OnabotulinumtoxinA Treatment of the Upper Face

Indication	Target Muscle	Preferred Injection Level	Injection Points (n)	Typical OnabotulinumtoxinA Dose per Injection Point	Typical Total Dose of OnabotulinumtoxinA
Glabellar lines	Procerus, corrugator supercilii, orbicularis oculi, depressor supercilii	Intramuscular	3 to 7	2 to 4 U	12 to 40 U; doses as low as 8 U may be appropriate for some patients
Horizontal forehead lines	Frontalis; consider interactions with procerus, corrugators, and orbicularis oculi in dosing, and effect on shape of the brows	Intramuscular or intracutaneous	4 to 8 (nonmicrodroplet) 8 to 20 (microdroplet)	2 to 4 U (nonmicrodroplet) 0.5 to 1.5 U (microdroplet)	8 to 25 U
Lateral canthal lines	Orbicularis oculi; uppermost injection point can also provide brow elevation	Intracutaneous	1 to 5 per side	1 to 4 U	6 to 15 U per side; doses as low as 4 U may be appropriate for some patients
Brow elevation	Lateral: orbicularis oculi; injection point is superior to the uppermost injection point for lateral canthal lines, and typically at the hairline of the eyebrow Medial: procerus, corrugator supercilii, depressor supercilii, orbicularis oculi	Intramuscular	Lateral, 1 to 2 per side medial, 1 to 2	Lateral: 0.5 to 1 U Medial: 0.5 to 4 U	1 to 6 U

these regions.^{37–39,47–49} It was recognized that hyaluronic acid fillers also play an important role.

Compared with previous guidelines, the Global Aesthetics Consensus Group recommended lower minimum doses and numbers of injection points (e.g., three to seven injection points for the glabella with total dosage of 12 to 40 units in most cases, and doses lower than 12 units when indicated). The publications cited above for glabellar lines pertain to treatment at maximal frown. Two randomized, double-blind, placebo-controlled studies of mild glabellar lines in repose demonstrated effective elimination with a 20-unit dose of onabotulinumtoxinA.⁵⁰ A meta-analysis of four trials with 621 patients found that 20-unit treatment of glabellar lines resulted in sustained clinical benefit for 4 months in more than half of responders.⁵¹ Patient satisfaction increased with duration of effect.

For lateral canthal lines, some panelists suggested a reduction in dose per injection site for the inferior lateral orbicularis oculi and combined treatment with hyaluronic acid fillers to address lines that encroach inferiorly on the cheek. They

recommended avoidance of the second row of injections that was described previously for rhytides that extend toward the temporal hairline, considering volume loss as their primary etiology and with the aim of avoiding complications. Other panelists advocated a second row of injections for patients whose skin is severely sun damaged or who have undergone cosmetic surgery, such as face lifting with consequent extension of rhytides as far as the hairline.

For horizontal forehead lines, some panelists use intracutaneous injection, especially near the eyebrow, to achieve superficial delivery of toxin to the underlying frontalis with lower dose per unit volume of muscle. The objective is to modulate the depth and magnitude of effect, thus improving rhytides without causing eyebrow descent.

Midface: Infraorbital Rhytides, Nasal Oblique Lines, Nasal Flare, Nasal Tip Elevation, and Excessive Gingival Show

Clinical data pertaining to botulinum toxin type A alone for the midface are limited.^{52–54} The

Table 5. Consensus Recommendations and Expert Panel Opinions Regarding OnabotulinumtoxinA Treatment of the Midface

Indication	Target Muscle	Preferred Injection Level	Injection Points (n)	Typical OnabotulinumtoxinA Dose per Injection Point	Typical Total Dose of OnabotulinumtoxinA
Infraorbital rhytides	Orbicularis oculi	Intracutaneous	1 to 3 per side; microdroplet technique may be beneficial	0.5 to 2 U	0.5 to 2 U per side
Eye opening (lowering of inferior ciliary margin) ⁴⁸	Orbicularis oculi	Intracutaneous	1 per side; midpupillary line	0.5 to 1 U	0.5 to 1 U per side
Nasal flare	Dilator nasalis (alar portion of nasalis) Medial portion of levator labii superioris alaeque nasi may also be considered	Intramuscular	2	1 to 2 U	1 to 4 U
Nasal tip elevation	Depressor septi nasi	Intramuscular; often ancillary to fillers	1	2 to 6 U	2 to 6 U
Nasal oblique lines (bunny lines)	Nasalis; levator labii superioris alaeque nasi and depressor nasi septi should also be considered	Intramuscular	2 to 3	2 to 4 U	4–8 U; doses as high as 10 U may be appropriate for some patients
Excessive gingival show (gummy smile)	Convergence of levator labii superioris alaeque nasi and zygomaticus minor with insertion of levator labii superioris	Intramuscular	1 to 2 per side	0.5 to 2 U	1 to 4 U; doses as high as 8 U may be appropriate for some patients

2010 French consensus publication included multidisciplinary recommendations for prevention and treatment of rhytides in this region.⁷ In premeeting surveys, panelists reported using botulinum toxin alone for infraorbital rhytides in 49 percent of cases and in 42 percent of procedures for nasal lines, nasal flare, or nasal tip elevation (Fig. 1). Filler alone was the treatment of choice for the cheek.

The panelists recognized the contribution of the nasalis muscle to nasal oblique lines, the

current understanding that the levator labii superioris alaeque nasi often has a primary role, and that patterns of secondary muscle recruitment must be considered.²⁹ Several panelists considered use of botulinum toxin for nasal tip elevation to be ancillary to that of hyaluronic acid fillers, based on an understanding of the need to correct volume loss. Excessive gingival show (gummy smile) can be attributed to skeletal, gingival, and/or muscular factors.⁵⁴ When appropriate,

Table 6. Consensus Recommendations and Expert Panel Opinions Regarding OnabotulinumtoxinA Treatment of the Lower Face

Indication	Target Muscle	Preferred Injection Level	Injection Points (n)	Typical OnabotulinumtoxinA Dose per Injection Point	Typical Total Dose of OnabotulinumtoxinA
Depressor anguli oris overactivity	Depressor anguli oris	Intramuscular	1 to 2 per side	2 U	2 to 4 U per side; some panelists limit dose to 2 U per side
Mentalis overactivity	Mentalis	Intramuscular	1 to 4 per side	2 to 3 U	4 to 10 U
Masseter overactivity	Masseter	Intramuscular	1 to 5 per side	5 to 15 U	15 to 40 U
Perioral rhytides	Orbicularis oris	Intracutaneous; ideally, intradermal	2 to 5	0.5 to 1 U	1 to 5 U
Platysmal bands	Platysma	Intramuscular or intracutaneous	3 to 6 per band	1 to 3 U	6 to 12 U per band; maximum dose 60 U

Table 7. Global Aesthetics Consensus Group Recommendations and Position Statements for Botulinum Toxin Type A

Consensus recommendations for injection sites and dosage when treating the upper, middle, and lower face and neck regions with onabotulinumtoxinA are provided in Tables 4 through 6. Recommendations may be extrapolated with care, and appropriate dosages, to other botulinum toxin formulations.	R
Integrated assessment of target and adjacent musculature should be performed in the context of associated soft and hard tissues, and of the whole face, to inform treatment planning and implementation for each region.	R
Pretreatment assessment should be performed in repose and in animation. Assessment when the patient is engaged in routine activities such as speaking (informal assessment) is frequently of more value than assessment during animation on command (formal assessment).	R
Although botulinum toxin alone is often appropriate, especially for the upper face, combination treatment with hyaluronic acid fillers is increasingly recognized as having potential to optimize outcomes. The appropriateness of combined treatment should be considered for all regions, including the upper face.	R
The performance of skin snap and stretch tests as part of pretreatment assessment aids in evaluation of tissue quality and etiology of rhytides and, hence, in determination of the appropriate treatment plan.	R
Anatomically appropriate landmarks to guide injection points for botulinum toxin are muscular and bony. Skin landmarks should not be used.	R
Removal of makeup; scrupulous skin cleansing before, during, and after injection; and sterile injection technique are recommended to minimize the risk of avoidable contamination.	R
Formulations of currently available botulinum toxin type A products are unique, their doses are not interchangeable, and the dose response curves are probably not parallel.	R
The concentration of botulinum toxin may be titrated, based on the facial region to be treated and the desired outcome (e.g., degree of postinjection spread).	PS
Intracutaneous injection may limit depth of effect and be of use where partial inactivation of muscular activity is desired (e.g., to achieve neuromodulation rather than paralysis).	PS
The response rate to botulinum toxin type A is very high; partial or complete nonresponse occurs rarely. In cases of apparent nonresponse, practitioners should first consider the possibility of inappropriate patient selection, inadequate dosing, or incorrect placement of injection sites.*	PS
More clinical studies of botulinum toxin are needed, especially in the midface and lower face.	PS
Although most patients who seek treatment are between the ages of 30 and 50 years, extension of treatment to patients outside this age range can be beneficial (e.g., to younger patients in the presence of congenital or acquired facial disharmonies, or for preventive purposes)*.	R
More clinical studies are needed to differentiate and determine the efficacy of treatment strategies related to patient ethnicity, gender, and age.*	PS

R, recommendation; PS, position statement. *These considerations are discussed further in another publication in the Global Aesthetics Consensus Group series (Global Aesthetics Consensus Group: Hyaluronic Acid Fillers and Botulinum Toxin Type A: Recommendations for Combined Treatment and Special Considerations to Optimize Outcomes in Diverse Patient Populations).

botulinum toxin can effectively target overactive lip elevator muscles.

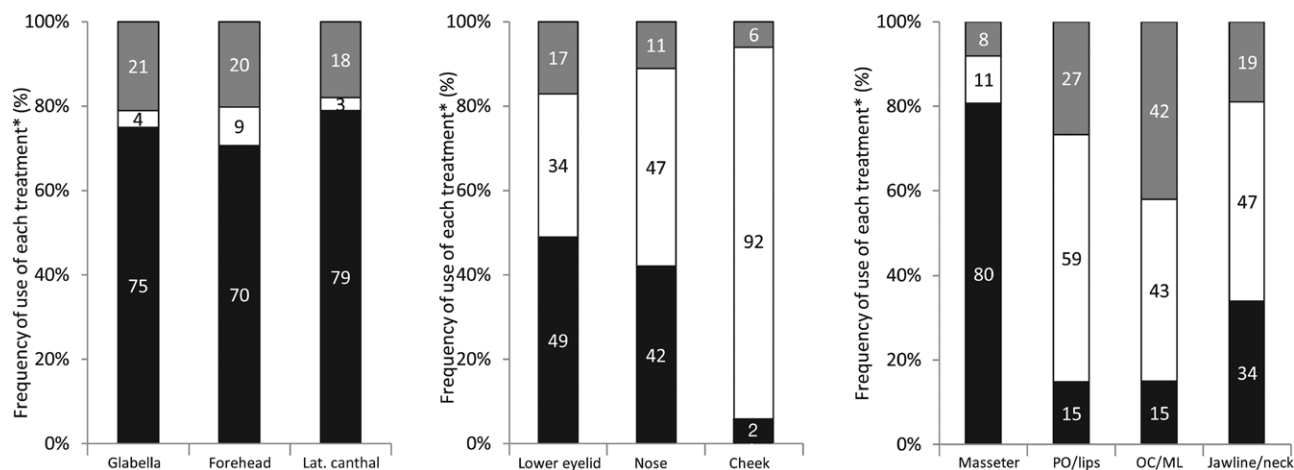
Lower Face and Neck: Depressor Anguli Oris, Mentalis, Masseter, Perioral Rhytides, and Platysmal Bands

Previous guidelines focused on the benefits of combining hyaluronic acid fillers and botulinum toxin type A for the lower face.⁶ Recent clinical trials demonstrated the efficacy and safety of combination therapy for lower facial rejuvenation, with better results than either modality alone.^{56,57} Although there are limited data for treatment of the lower face and neck with botulinum toxin alone,^{58–60} clinical use is well documented. On the basis of premeeting surveys, Figure 1 summarizes the panelists' use of botulinum toxin alone, combined treatment with fillers, and fillers alone.

The panel recommended a range of injection sites, dosages per injection site, and total doses in treatment of the masseter, depending on the objective (e.g., reduction of hypertrophy as a result

of bruxism versus facial tapering for aesthetic reasons). To determine the appropriateness of toxin treatment, clinicians were advised to distinguish true masseteric hypertrophy from parotid gland hypertrophy or masseteric prominence as a result of volume loss, and to identify pathology such as parotid swelling related to Sjögren syndrome or bulimia nervosa.⁶¹

The Global Aesthetics Consensus Group recommendations for orbicularis oris and for platysmal bands represent lower dosing than originally described. A limited and carefully selected population of patients can benefit from treatment of platysma from the mandibular border to the corner of the mouth (Neferiti neck lift) to weaken the depressor action of platysma and hence produce relative augmentation of elevator action. These patients typically have good retention of tissue quality and palpable platysmal muscle mass, especially posteriorly, with a band that obscures the mandibular border when platysma is contracted while the patient is seated.



PO = perioral; OC/ML = oral commissure or marionette lines. *Percentages are rounded to the nearest whole number and may not add up to 100 due to rounding.

■ Botulinum toxin Type A alone □ Filler alone ■ Botulinum toxin Type A + Filler

Fig. 1. Practice patterns of the consensus panel in the upper face (left), midface (center), and lower face (right) based on premeeting surveys. Percentage use of botulinum toxin type A alone, filler alone, and botulinum toxin type A plus filler is shown for each facial zone. PO, perioral; OC/ML, oral commissure or marionette lines. Black, botulinum toxin type A alone; white, filler alone; gray, botulinum toxin type A plus filler. *Percentages are rounded to the nearest whole number and may not total 100 because of rounding.

CONTRAINDICATIONS, AVOIDANCE OF COMPLICATIONS, AND POSTTREATMENT RECOMMENDATIONS

Based on clinical experience, retrospective reviews, and meta-analyses, botulinum toxin type A has excellent safety and tolerability profiles across a spectrum of aesthetic and therapeutic applications.⁶²⁻⁶⁴ Table 8 presents some potential adverse events from aesthetic use. Their incidence can be minimized through following the guidelines in this publication regarding appropriate selection of patients, injection strategies, and dosages. A recent systematic review of

31 randomized or open-label clinical studies of botulinum toxin type A in aesthetic treatments quantified the incidence of treatment-related blepharoptosis (2.5 percent), brow ptosis (3.1 percent), eye sensory disorders (3 percent), and lip asymmetries and imbalances of the lower face (6.9 percent).⁶² Treatment-related adverse events were considered secondary to “excessive action of the drug,” or “diffusion to nearby unwanted targets.” OnabotulinumtoxinA was used in 60.0 percent of these studies, abobotulinumtoxinA in 37.1 percent, and incobotulinumtoxin in 2.8 percent of cases. A retrospective review from 2008 to 2013 of an American Society of

Table 8. Some Potential Adverse Events from Aesthetic Use of Botulinum Toxin Type A*

Upper face and midface

- Asymmetry
- Ptosis of eyebrow or eyelid
- Unmasking of preexisting, compensated eyelid ptosis (weakening of frontalis)
- Impairment of eyelid function/ocular physiology (weakening of orbicularis oculi)
- Lower lid retraction/scleral show (weakening of orbicularis oculi)
- Lip ptosis (weakening of lip elevators when addressing nasal indications)
- Atrophy

Lower face

- Asymmetry
- Oral motor insufficiency, e.g., impaired ability to raise or lower the lip
- Impairment of dental show in animation (smiling)
- Impaired muscular support of lower face
- Dysphagia (when targeting platysma)
- Neck weakness (when targeting platysma)
- Dry mouth (when targeting platysma)

*Temporary ecchymosis, hematoma, or edema/swelling may occur after injection in any facial region.

Plastic Surgeons–endorsed database reported that patients older than 65 years of age had significantly more cosmetic facial procedures performed than younger patients (62.9 percent versus 12 percent). The complication rate after all procedures in the older group (mean age, 69.1 years; 1.94 percent) was statistically insignificant compared with that in the younger group (mean age, 39.2 years; 1.84 percent). This was despite the greater presence of higher body mass index, incidence of diabetes mellitus, and other health risks in the older group.⁶³

General strategies to prevent complications from botulinum toxin type A injection are well described in previous guidelines.^{6,9} The consensus panel noted growing realization that injection of toxin or filler is a minor surgical procedure from the perspective of pretreatment preparation. No procedure that breaches the skin surface can ever be sterile. Removal of all makeup, scrupulous skin cleansing before, during, and after injection, and sterile injection technique (including avoidance of injection through bacteria-rich fields such as hair follicles) are recommended to minimize avoidable contamination. Although it is desirable for patients to avoid anticoagulants, nonsteroidal anti-inflammatory drugs, fish oil supplements, and other agents that could increase postprocedural ecchymosis, use of these products is not a contraindication to treatment. Brief application of cold packs or ice to the treatment area after injection can help to minimize swelling and bruising. The consensus panel found no evidence to support previous posttreatment recommendations regarding avoidance of pressure on injected areas, strenuous exercise, or air travel.

SUMMARY AND CONCLUSIONS

The Global Aesthetics Consensus Group recommendations for botulinum toxin type A treatment of the face and neck are based on the accumulation of clinical experience and study data. Key recommendations include:

- An individualized, integrated approach to assessment and treatment planning.
- Selection of botulinum toxin as a primary treatment only if the target muscle is the primary etiology of the facial disharmony to be addressed.
- Analysis of target muscles in the context of adjacent muscles and associated soft and hard tissues.

- Lower doses for the upper face and some regions of the lower face.
- Intracutaneous injection, where indicated to limit depth and magnitude of effects.
- More frequent combination of toxin with fillers for all facial regions, including the upper face.

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