Noninvasive Facial Rejuvenation. Part 2: Physician-Directed—Neuromodulators and Fillers

Ryan M. Dickey, BM¹ Matthew R. Louis, BS¹ Joshua A. Cox, MD¹ Kriti Mohan, MD¹ Edward I. Lee, MD¹
Marjory G. Nigro, MD²

¹Division of Plastic Surgery, Department of Surgery, Baylor College of Medicine, Houston, Texas

²Nigro Dermatology Group, Houston, Texas

Address for correspondence: Marjory G. Nigro, MD, Nigro Dermatology Group, 2800 Kirby Dr., Suite A-200, Houston, TX 77098 (e-mail: marjory@swbell.net).

Semin Plast Surg 2016;30:134–142.

Abstract

A proper knowledge of noninvasive facial rejuvenation is integral to the practice of a cosmetic surgeon. Noninvasive facial rejuvenation can be divided into patient- versus physician-directed modalities. Patient-directed facial rejuvenation combines the use of facial products such as sunscreen, moisturizers, retinoids, α -hydroxy acids, and various antioxidants to both maintain youthful skin as well as rejuvenate damaged skin. Physicians may recommend and often prescribe certain products, but patients are in control with this type of facial rejuvenation. On the other hand, physician-directed facial rejuvenation entails modalities that require direct physician involvement, such as neuromodulators, filler injections, laser resurfacing, microdermabrasion, and chemical peels. With the successful integration of each of these modalities, a complete facial regimen can be established and patient satisfaction can be maximized. This article is the second in a three-part series describing noninvasive facial rejuvenation. Here the authors discuss neuromodulators and fillers in detail, focusing on indications for use, techniques, and common side effects.

Keywords

- ▶ neuromodulators
- ▶ fillers
- ▶ noninvasive facial rejuvenation

Botulinum toxin A (BONT-A) and soft tissue fillers have become the dominant form of noninvasive facial rejuvenation. Botulinum toxin injection has become the most widely used minimally invasive cosmetic procedure with a 759% increase in the past 15 years.¹ In conjunction with the rising use of BONT-A, soft tissue fillers have also become more prevalent with a 274% increase in the past 15 years.¹ Considering the rising demand for these products, it is of utmost importance for a plastic surgeon to be well versed on this topic. The purpose of this review is to inform and educate practitioners on the use of these two noninvasive facial rejuvenation techniques, including injection techniques and common complications that may be encountered.

Botulinum Toxin A

Mechanism of Action

Produced by the gram-positive rod *Clostridium botulinum*, BONT-A inhibits the presynaptic release of acetylcholine at the neuromuscular junction, effectively diminishing the focal

contraction of muscle units. A more youthful appearance is achieved by the selective weakening of the muscles underneath rhytides. As such, rhytides that are caused by underlying muscle contraction tend to have greater response to the injection than those caused by the thinning of the dermis and elastosis. Through the years, the use of BONT-A in cosmetic procedures has evolved from being used primarily for the upper face (i.e., glabellar lines, crow's feet, and forehead lines) to the lower face.²

Formulas, Distribution, and Storage

The two most potent and widely used BONTs are BONT-A and BONT-B. The only BONT-B approved for use by the Food and Drug Administration (FDA) is rimabotulinumtoxinB (Myobloc; Solstice Neurosciences, LLC); it is approved for the treatment of cervical dystonia. The three FDA-approved cosmetic BONT-A drugs are onabotulinumtoxinA (Botox Cosmetic; Allergan, Inc.), abobotulinumtoxinA (Dysport; Galderma Laboratories), and incobotulinumtoxinA (Xeomin;

Merz Pharma). Botox was first approved by the FDA in 2002 for the temporary reduction of glabellar lines associated with corrugator and procerus activity in patients under 65 years old, with Dysport approval following in 2009 and Xeomin in 2011. In 2013, the FDA approved Botox for the treatment of lateral canthal lines (or crow's feet).

Botox is distributed as a powder in either 50 U or 100 U in a single-use vial. Dysport is distributed in 300 U and 500 U vials. Of note, the "units" of Botox and Dysport are not a 1:1 conversion. Studies suggest that 1 U of Botox is roughly equivalent to 2.5 to 5 U of Dysport.^{3,4} Both products can be reconstituted in either preserved 0.9% saline or nonpreserved 0.9% saline according to the dilution provided in the package insert. Preserved saline is the preferred solution and has been found to decrease pain on injection site in at least five randomized controlled trials.^{5–9} Botox is most commonly reconstituted with 2.5 cc of preserved saline for a 100 U bottle and 1.25 cc for a 50 U bottle, yielding an injection volume standard of 4 U per 0.1 cc. Once reconstituted, immediate use is suggested; however, some clinicians have used the products as many as 5 to 7 days later.^{10,11} A consensus statement released by Alam et al in 2015 stated that "a vial of BONT-A can be refrigerated or frozen for at least 4 weeks before injection without clinically significant risk for contamination or decreased effectiveness." In addition, they

found that a single vial can be used to treat multiple patients.¹²

Dosage

The dosage of BONT depends on numerous factors, including injection site, patient sex, previous effective dosage, and clinician preference. ►Table 1 provides dosages for each functional anatomical unit based on the consensus guidelines of Sundaram et al.¹³ Our recommended Botox injection procedures to the upper face in women and men, respectively, are illustrated in ►Figs. 1 and 2. Both the table and the figures should be used as general guidelines—with more importance given to past successful doses for each patient in addition to clinical judgment. For instance, men often have more muscle mass, thus requiring an increased dosage compared with women.¹⁴ To this end, keeping an injection log can be helpful in determining the outcome of each injection as well as improve upon the success of subsequent injections (►Fig. 3).

In recent years, the recommended dosage of BONT-A has shifted to lower doses for virtually all aspects of the face. This may be due to patients' preference for a more natural appearance or it may be due to increased physician experience.¹³ In addition, evidence suggests that the overall dosage per patient over time is consistent. Carruthers et al found that over a 5 year or more time period, the dosage of Botox

Table 1 Botulinum toxin A injection guidance by anatomical region

Regions injected	Number of injections used	Total dosage
		OnabotulinumtoxinA (Units)
Upper face		
Vertical frown lines, glabellar region	3 to 7	W: 10–30; M: 20–40
Horizontal forehead lines	4–8	W: 6–15; M: 6–15
Lateral canthal lines	2–5	6–15 per side
Brow elevation	Lateral 1–2; medial 1–2	1–6
Midface		
Radix	1–2	2–4
Nasal tip	2–4	3–5
Infraorbital rhytides	1–3 per side	0.5–2
Eye opening	1 per side	0.5–1
Nasal flare	2	1–4
Nasal tip elevation	1	2–6
Nasal oblique lines	2–3	4–10
Gummy smile	1–2 per side	1–8
Lower face		
Depressor anguli oris	1–2 per side	2–4
Mentalis	1–4 per side	4–10
Masseteric hypertrophy	1 to 5 per side	15–40
Perioral rhytides	2–5	1–5
Platysmal bands	3–6 per band	6–12; max of 60

Abbreviations: W, women; M, men.

Source: Adapted from Sundaram et al.¹³

Fig. 1 Our recommended upper face onabotulinumtoxinA (Botox Cosmetic; Allergan, Inc.) injection in women.

remained approximately equal, while the interinjection time period increased.² As the medical community has become more familiar with the use of BONT-A, selective weakening as opposed to paralysis of the targeted muscle has become the favored physiological result.

Two phases of botulinum action are to be expected. The first is “spread,” which is directly related to the events surrounding injection, such as injection depth, rate, volume, and needle size. “Diffusion” is the second phase and is the byproduct of natural diffusion of the toxin through tissue

away from the high concentration at the local injection site.¹⁵ Botox and Dysport act for approximately 3 to 4 months, though interpatient variation exists.

Technique

Proper injection technique is paramount to achieving optimal results. Before injecting into each anatomical unit, the patient’s natural animation should be evaluated. Appreciation of variance in facial anatomy will lead to more satisfied patients as well as a more natural postinjection appearance.

Fig. 2 Our recommended upper face onabotulinumtoxinA (Botox Cosmetic; Allergan, Inc.) injection in men.

INJECTION SITE RECORD

Compliments of ALLERGAN

PATIENT NAME:

CHART #/ IDENT:

		AREA 1	AREA 2	AREA 3	AREA 4
Treatment Date					
	Dilution (mL)				
	Units / 0.1 mL				
Location					
Lot Number					
Expiration Date					
Total Units / Site					
	Site A				
	Site B				
	Site C				
	Site D				
Total Units Used					

PATIENT HISTORY:

NOTES:

Fig. 3 Botulinum toxin injection record (with permission, Botox Cosmetic; Allergan, Inc.).

The following general principles should be applied in each region.

In the forehead, overinjection can lead to an undesirable artificial appearance and the risk of brow and eyelid ptosis. To minimize these risks, the patient should be asked to elevate and depress the brow so that the strongest portions of the frontalis are targeted for denervation.¹⁶

In addressing the glabellar musculature, the clinician should ask the patient to alternate between frowning and scrunching her or his nose. If movement is primarily in a vertical fashion, injections are made in the medial aspect of the corrugator, procerus, and nasalis muscles. Patients with primarily horizontal movement should not be injected in the procerus muscle.¹⁶ When injecting into the glabella, the bevel of the needle should be oriented away from the orbits (► **Fig. 4**).

To correct crow's feet, the injection sites should be superficial and 1.0 to 1.5 cm lateral to the lateral orbital rim and superior to the zygomatic arch. This technique will reduce the risk of diplopia, ectropion, and smile asymmetry.¹⁶

The manipulation of brow elevation involves chemodenervation of the brow depressors. One must also consider the resultant comparatively overactive muscle groups that were not chemodenervated. Selective medial brow elevation is achieved by weakening the medial depressors and lateral frontalis while sparing the medial frontalis. On the contrary, selective lateral elevation involves eliminating the lateral depressor and weakening the opposing medial frontalis. In addition, the tail of the brow can be raised by approximately 0.5 cm by injecting 2 U into the lateral orbicularis oculi at the junction of lateral brow and the medial edge of the temporal

Fig. 4 Pre- and post-botulinum toxin injection to forehead and glabella.

bone. In cases of asymmetrical brow elevation, the frontalis is injected over the higher brow, allowing the uninjected frontalis of the relatively depressed brow to be elevated.

Botulinum toxin can also be used to manipulate the lower eyelid as well as the aperture of the eye. To create a more rounded eye, 2 U of Botox can be injected into the lower eyelid, approximately 1 mm below the lash line at the mid-pupillary line. The injection should be superficial and parallel to the skin. Patients should be counseled on the possibility of dry eyes with this injection. Moreover, this injection is generally indicated for younger patients as injection in a patient with lax orbicularis can lead to ectropion.

Patients with prominent platysmal bands can also be considered for BONT injection. Particularly well-suited candidates include patients with little excess skin and projecting bands as well as postoperative neck- and facelift patients with recurrent bands. The patient should be asked to simultaneously display the lower teeth while clenching his or her jaw. The band should be grasped and the patient can relax. Injections should begin below the jaw line and continue inferiorly.

In patients seeking injection of the nasolabial folds, the clinician should first assess the smile pattern of the patient. Often, patients with “canine” (the central upper lip is the most superior portion of the smile) or “gummy” (more pronounced canine smile) smile seek the classic “Mona Lisa” smile where the oral commissure is the most cephalad portion of the smile, produced by action of the zygomaticus muscle. In patients with either a “canine” or “gummy” smile, the levator labii superioris elevates the central upper lip to the most superior part of the smile. Injection of the levator labii superioris alaeque nasi bilaterally results in relaxation of the central upper lip, effectively converting the canine smile to the “Mona Lisa” smile. Those with gummy smiles often have asymmetric smiles, thus nonequal dosages are required on each side.¹⁶

Patients seeking elimination or reduction of perioral lines are most likely to fall into one of three categories: (1) those who are already getting Botox elsewhere, (2) those who do not like the

“look” of fillers, and (3) those who desire both fillers and neuromodulators. In the latter group, fillers function to restore volume while neuromodulators relieve tension on the skin of the upper lip by denervating the orbicularis oris muscle. Great care must be taken in the perioral region to avoid undesirable side effects such as difficulty with speech (inability to generate plosive sounds) as well as oral competence. Overzealous and unguided injection of the lower lip can lead to the disastrous side effects of oral incompetence and unsightly drooling.¹⁶

Injection of the depressor anguli oris raises oral commissures, thus reducing the visibility of the lower teeth and improving marionette lines. It is not advisable to inject into the most cephalad portion of the depressor anguli oris as there is little active muscle in that region. Additionally, injection of the lower orbicularis oris often leads to oral incompetence and drooling.¹⁶

Contraindications

Contraindications for the use of BONT include conditions affecting the neuromuscular junction (myasthenia gravis and Lambert-Eaton), aminoglycoside use, infection at the injection site, previous reaction to BONT use, and pregnancy. In addition to the site-dependent side effects described above, infection, inflammation, pain, erythema, ecchymosis, and weakness may result, but are rare. One of the most common cosmetic side effects is an unintended “Mephisto” brow (the lateral aspect of the eyebrow is superior to the medial aspect creating a quizzical look) and lip weakness. Carruthers et al found these local facial muscle events to occur in 11.1% of patients, most commonly in the first 2 years of treatment.² These side effects may be avoided by using proper injection techniques together with careful attention to facial anatomy. In the upper face, the “danger zone,” which is an area within 2 cm above the eyebrow from the midpupillary line to the tail of the brow, should not be injected as this will lead to brow ptosis (► Fig. 5). For any residual fine lines and wrinkles, fillers should be preferentially used in this area to minimize complications.

Fig. 5 Upper face danger zone for botulinum toxin injection.

Outcomes and Satisfaction

Provided that proper technique is adhered to, patient satisfaction is remarkably high. In a 2015 study by Carruthers et al, the role of neuromodulators in a facial aesthetic regimen was evaluated over a 5-year period. Using the validated Facial Line Satisfaction Questionnaire Follow-Up Version, the group found that 98.3% of patients younger than 50 years were very satisfied or mostly satisfied with their results, 91.9% for those aged 50 to 59, and 87.8% for those aged 60 or older. Patients who received their first treatment at age 55 or older perceived themselves to have a mean reduction in perceived age of 7.3 years, whereas those who received their treatment before 35 years of age perceived themselves to be 4.9 years younger.²

The past 20 years has witnessed an explosive increase in the use of BONT for cosmetic plastic surgery. As more studies are conducted and physicians become more experienced with the emerging techniques, patient satisfaction will increase and even more creative uses for BONT may be found.

Fillers

As the use of neuromodulators has advanced, so too has the use of fillers. These are not competing techniques, but rather complementary methods to create a balanced facial cosmetic regimen. When used together appropriately, patient satisfaction and outcomes can be optimized.

Types

Several types of injectable soft tissue fillers exist, including autologous fat, hyaluronic acid, Radiesse, Sculptra, and Arte-fill.^{17–19} First described in 1893, autologous fat is by far the oldest injectable filler.²⁰ Although abundant and biocompatible, its permanency varies greatly and thus various techniques have been described for harvesting, processing, and grafting. Outcomes are best when injecting multiple passes

of small aliquots, providing for diffuse infiltration to increase contact with the native vascular bed. Grafted fat stabilizes around 4 months after the procedure, but may continue to attenuate for up to 1 year.

Currently, the most widely used filler is hyaluronic acid.¹ Hyaluronic acid is a naturally occurring glycosaminoglycan polymer present in all connective tissue. It is the most common filler used mainly because of its ease of use and the ability to improve facial volume with a proven safety profile and a decreased risk of hypersensitivity reaction, negating the need for preprocedure skin testing that is required for older, collagen-based products. Its clinical effect can last up to 9 months (►Fig. 6). There are multiple manufacturers of hyaluronic acid. The Restylane and Perlane products (Galderma Laboratories) are intended for varying depths and utilize different-sized particles. Compared with the concentration of Restylane (20 mg/mL), Juvéderm (Allergan, Inc.) contains a higher concentration of hyaluronic acid (24 mg/mL), increasing filler cross-linking with increased duration of effect for up to 12 months. Restylane-L, Restylane Silk, Perlane-L, Juvéderm XC, and Prevelle Silk (Mentor Corp.) contain lidocaine for reduced procedural pain. In addition, each hyaluronic acid filler has a specific profile based on anatomical regions, patient skin type, and preference (►Table 2).

Radiesse (Merz Aesthetics, Inc.) consists of calcium hydroxylapatite that serves as a scaffold for native collagen growth. Deep injection is recommended due to its high viscosity and propensity for nodule formation, particularly in the lips. Duration of effect typically ranges from 9 to 18 months, although it can last up to 2 to 5 years.

Sculptra (Galderma Laboratories) is an injectable poly-L-lactic acid constituted from microspheres in powder form. It serves to stimulate fibroblasts and growth of type I collagen resulting in soft tissue augmentation. Sculptra is used best as a volumetric filler, and often requires multiple deep injections

Fig. 6 (A) Pre- and (B) post-hyaluronic acid injection for lower eyelid rejuvenation.

for optimal effect (→ **Fig. 7**). Duration of effect ranges from 18 to 24 months. Similar to Radiesse, it is prone to nodule formation, although this can be mitigated with deep injection, high volume reconstitution over 5 mL, and overnight reconstitution times. In addition, postinjection massage (“Rule of 3s”—3 massages a day, for 3 days, for 3 minutes) can be helpful in minimizing nodules. An office staff member should perform the first massage so that the patient can learn the proper technique. Taking an anti-inflammatory 30 minutes prior to massaging can mitigate pain and improve compliance. Poly-L-lactic acid was specifically approved for the treatment of facial lipodystrophy syndrome associated with treatment for human immunodeficiency virus (HIV), though it is now used for the

general population as well. Results from treating lipodystrophy appear to be long lasting with high patient satisfaction.^{21,22}

Bellafill (Suneva Medical, Inc.), formerly known as Artefill, consists of polymethylmethacrylate (PMMA) microspheres (20% by volume) that are 30 to 50 μm in diameter, and suspended in a 3.5% bovine collagen solution (80% by volume) and 0.3% lidocaine.²³ The proposed mechanism of Bellafill is the stimulation of autologous collagen, which then envelops the PMMA microspheres permanently. Due to its bovine composition, patients must be skin tested for hypersensitivity at least 1 month prior to injection. It is currently FDA approved for nasolabial fold injection. Of note, it should not be used in patients at risk for keloid formation or hypertrophic scarring.²⁴

Table 2 Hyaluronic acid facial filler: Manufacturer characteristics

Filler brand	Cross-linking agent	Concentration	Indications
Restylane (Galderma Laboratories)	BDDE	20 mg/mL (250 μm size)	Mid-to-deep dermal implantation for severe facial wrinkles, submucosal implantation for lip augmentation
Restylane-L (Galderma Laboratories)	BDDE	20 mg/mL with 0.3% hyaluronic acid (250 μm size)	Mid-to-deep dermal implantation for severe facial wrinkles, submucosal implantation for lip augmentation
Restylane Silk (Galderma Laboratories)	BDDE	20 mg/mL with 0.3% hyaluronic acid (250 μm size)	Submucosal implantation for lip augmentation, dermal implantation of perioral rhytides
Perlane (Galderma Laboratories)	BDDE	20 mg/mL, (750–1,000 μm size)	Deep dermal implantation for severe facial wrinkles
Perlane-L (Galderma Laboratories)	BDDE	20 mg/mL with 0.3% hyaluronic acid, (750–1,000 μm size)	Deep dermal implantation for severe facial wrinkles
Juvéderm Ultra XC (Allergan, Inc.)	—	24 mg/mL with 0.3% lidocaine	Mid-to-deep dermis for moderate to severe facial wrinkles, lip augmentation
Juvéderm Ultra Plus XC (Allergan, Inc.)	—	24 mg/mL with 0.3% lidocaine	Mid-to-deep dermis for moderate to severe facial wrinkles
Juvéderm Ultra (Allergan, Inc.)	—	24 mg/mL	Mid-to-deep dermis for moderate-to-severe facial wrinkles
Juvéderm Ultra Plus (Allergan, Inc.)	—	24 mg/mL	Mid-to-deep dermis for moderate-to-severe facial wrinkles
Juvéderm Voluma XC (Allergan, Inc.)	—	20 mg/mL with 0.3% lidocaine	Subcutaneous and/or supraperiosteal injection for cheek augmentation

Abbreviations: BDDE, 1,4-butanediol diglycidyl ether.

Fig. 7 (A) Pre- and (B) post-Sculptra (Galderma Laboratories) injection for lower face rejuvenation.

Technique

Strict attention to sterile technique is essential when administering all fillers, as contamination of the foreign filler material leads to infection that is difficult to treat secondary to biofilm formation.²⁵ For skin preparation, chlorhexidine may have the advantage of residual antimicrobial effect compared with alcohol, although either may be used. Chlorhexidine should be avoided in the periorbital region due to the risk of keratitis. The skin should also be taut during sterilization to ensure sterilization of wrinkle crevices.

For analgesia during the procedure, either topical anesthetics or combinations of filler and anesthetic may be used. In general, the smallest possible needle that is able to adequately deliver the relative viscosity of the filler should be used. For example, less-viscous fillers such as hyaluronic acid may allow use of 30-g needles, 27-g needles accommodate intermediate viscous fillers such as calcium hydroxylapatite, and highly viscous fillers such as poly-L-lactic acid may require 25-g needles. A visual rule of thumb may reveal the depth of injection. When using a 26-g needle, the gray of the needle may be seen at intradermal depth, and the shape of the needle may be seen at superficial subdermal depth; the subdermal fat is depressed with the tip of the needle at deep subdermal depth.²⁴

Several injection techniques may be used during filler administration, including serial puncture or droplet, linear threading, fanning, and crosshatching. Linear threading is generally safer, but each technique has its own advantages and is appropriate for certain anatomical regions. For the glabellar region, philtral columns, and fine rhytides, the serial puncture or droplet technique is favored, consisting of small injections made in multiple sequences along a wrinkle. For the nasolabial fold and vermilliocutaneous border, linear threading is best. In this technique, the filler is deposited while simultaneously advancing (anterograde) or withdrawing (retrograde) the needle, creating a line of filler as opposed

to a small droplet as in the serial puncture technique. Anterograde linear threading may provide a less-painful experience and decreased bruising, while retrograde linear threading is better suited for intravascular regions, such as the glabella. For the nasolabial fold, fanning is the most suitable, and consists of a single-needle insertion with multiple passes in varying directions and layers without withdrawing the needle. For large areas and the oral commissures, crosshatching provides the most volume and consists of injecting an evenly spaced grid. Ideally, multiple or deep injections are preferred to large volumes in the subepidermis, as the latter increases local adverse events.²⁴

Complications

Injectable complications are rare and many may be mitigated by meticulous technique and preparation. Early complications are mediated by acute inflammation and technical factors; late complications occur from granuloma formation and infection. Injection-site reactions may simply be treated with a cold compress. Superficial injection or an inappropriate high volume of injection is common and may lead to noticeable papules or edema. Prevention is crucial by utilizing as fine of a needle as possible and by discriminating the depth of the tip of the needle through ongoing training. Immediate massage or hyaluronidase, if hyaluronic acid filler was placed, may be used if papules appear. A particularly common scenario for overcorrection is the treatment of subocular lines with filler placed erroneously above the infraorbital rim, leading to persistent lid edema requiring hyaluronidase treatment. For more serious local allergic reactions, antihistamines, topical immunomodulators, and steroid injections may limit ongoing reactions. In patients with a history of herpes, prophylactic antiviral treatment should be considered when injecting around the lips as outbreaks may be triggered following injection.

Serious early complications include vascular compromise and necrosis, with an incidence of up to 3 in 1,000.²⁶ Ischemia

occurs in one of two ways, either by intra-arterial injection and occlusion with filler, or external compression of venous outflow. Such serious complications can be avoided by following sound technical principles, such as aspirating before injection, injecting slowly, and avoiding bolus injections. In the case of suspected ischemia, immediate warm gauze, nitroglycerin paste, and hyaluronidase injection should be used.

Chronic complications include granulomas, migration, scarring, and biofilms. Granulomas occur when activated macrophages induce chronic inflammation of the filler foreign body. Sterile abscess may also be present near such nodules, and should be suspected if there is no improvement on antibiotics for fluctuance or if cultures remain negative. Steroid injection at the site of the granuloma nodule is a proven therapy. A test response for treatment of granuloma formation may be performed on the forearm before further facial injection.²⁵

Although immediate infection occurring after inoculation of skin flora by injection may be treated with broad-spectrum antibiotics, delayed infections caused by biofilms are more challenging to treat. Biofilms consist of organisms encapsulated in polysaccharide matrix and are thus poorly penetrated by typical oral antibiotics. As proposed by Rohrich et al, if infection is suspected, any fluctuance should be drained and cultured, followed by two-drug therapy of a quinolone and macrolide. Hyaluronidase should be applied, or intralesional steroid if hyaluronic acid was not used.²⁴

Conclusion

Botulinum toxin A and soft tissue fillers have established themselves as the primary modalities of noninvasive facial rejuvenation. These are best thought of as synergistic tools instead of competing therapies for the cosmetic surgeon. A thorough understanding and application of these two techniques is essential for the practitioner. Applying these principles, patient expectations can be managed and satisfaction can be maximized.

References

- 1 American Society of Plastic Surgeons. Plastic Surgery Statistics Report. 2015 Cosmetic Plastic Surgery Statistics. 2015. Available at: <http://www.plasticsurgery.org/Documents/news-resources/statistics/2015-statistics/cosmetic-procedure-trends-2015.pdf>. Accessed February 15, 2016
- 2 Carruthers A, Sadick N, Brandt F, et al. Evolution of facial aesthetic treatment over five or more years: a retrospective cross-sectional analysis of continuous onabotulinumtoxinA treatment. *Dermatol Surg* 2015;41(6):693–701
- 3 Matarasso SL. Comparison of botulinum toxin types A and B: a bilateral and double-blind randomized evaluation in the treatment of canthal rhytides. *Dermatol Surg* 2003;29(1):7–13, discussion 13
- 4 Carruthers J, Carruthers A. Botulinum toxin A in the mid and lower face and neck. *Dermatol Clin* 2004;22(2):151–158
- 5 Allen SB, Goldenberg NA. Pain difference associated with injection of abobotulinumtoxinA reconstituted with preserved saline and preservative-free saline: a prospective, randomized, side-by-side, double-blind study. *Dermatol Surg* 2012;38(6):867–870
- 6 Sarifakioglu N, Sarifakioglu E. Evaluating effects of preservative-containing saline solution on pain perception during botulinum toxin type-a injections at different locations: a prospective, single-blinded, randomized controlled trial. *Aesthetic Plast Surg* 2005;29(2):113–115
- 7 Kwiat DM, Bersani TA, Bersani A. Increased patient comfort utilizing botulinum toxin type a reconstituted with preserved versus non-preserved saline. *Ophthal Plast Reconstr Surg* 2004;20(3):186–189
- 8 van Laborde S, Dover JS, Moore M, Stewart B, Arndt KA, Alam M. Reduction in injection pain with botulinum toxin type B further diluted using saline with preservative: a double-blind, randomized controlled trial. *J Am Acad Dermatol* 2003;48(6):875–877
- 9 Alam M, Dover JS, Arndt KA. Pain associated with injection of botulinum A exotoxin reconstituted using isotonic sodium chloride with and without preservative: a double-blind, randomized controlled trial. *Arch Dermatol* 2002;138(4):510–514
- 10 Klein AW. Dilution and storage of botulinum toxin. *Dermatol Surg* 1998;24(11):1179–1180
- 11 Hexsel DM, De Almeida AT, Rutowsch M, et al. Multicenter, double-blind study of the efficacy of injections with botulinum toxin type A reconstituted up to six consecutive weeks before application. *Dermatol Surg* 2003;29(5):523–529, discussion 529
- 12 Alam M, Bolotin D, Carruthers J, et al. Consensus statement regarding storage and reuse of previously reconstituted neuromodulators. *Dermatol Surg* 2015;41(3):321–326
- 13 Sundaram H, Signorini M, Liew S, et al; Global Aesthetics Consensus Group. Global aesthetics consensus: botulinum toxin type A—evidence-based review, emerging concepts, and consensus recommendations for aesthetic use, including updates on complications. *Plast Reconstr Surg* 2016;137(3):518e–529e
- 14 Kane MAC. The long-term effects of Botox injections. The Aesthetic Meeting. Dallas, TX; 1998
- 15 Pickett A. Dysport: pharmacological properties and factors that influence toxin action. *Toxicon* 2009;54(5):683–689
- 16 Kane M. Botulinum toxin. In: Thorne CHM, Gurtney GC, Chung K, et al, eds. Grabb and Smith's Plastic Surgery. 7th ed. Philadelphia, PA: Lippincott Williams & Williams; 2013
- 17 Broder KW, Cohen SR. An overview of permanent and semipermanent fillers. *Plast Reconstr Surg* 2006;118(3, Suppl):7S–14S
- 18 Eppley BL, Dadvand B. Injectable soft-tissue fillers: clinical overview. *Plast Reconstr Surg* 2006;118(4):98e–106e
- 19 Carruthers JDA, Glogau RG, Blitzer A; Facial Aesthetics Consensus Group Faculty. Advances in facial rejuvenation: botulinum toxin type a, hyaluronic acid dermal fillers, and combination therapies—consensus recommendations. *Plast Reconstr Surg* 2008;121(5, Suppl):5S–30S, quiz 31S–36S
- 20 Neuber GA. Fettransplantation. *Chir Kongr Verhandl Deutsche Gesellschaft für Chirurgie* 1893;22:66
- 21 Levy RM, Redbord KP, Hanke CW. Treatment of HIV lipoatrophy and lipoatrophy of aging with poly-L-lactic acid: a prospective 3-year follow-up study. *J Am Acad Dermatol* 2008;59(6):923–933
- 22 Duracinsky M, Leclercq P, Armstrong AR, Dolivo M, Mouly F, Chassany O. A longitudinal evaluation of the impact of a poly lactic acid injection therapy on health related quality of life amongst HIV patients treated with anti-retroviral agents under real conditions of use. *BMC Infect Dis* 2013;13:92
- 23 Lemperle G, Knapp TR, Sadick NS, Lemperle SM. ArteFill permanent injectable for soft tissue augmentation: I. Mechanism of action and injection techniques. *Aesthetic Plast Surg* 2010;34(3):264–272
- 24 Nguyen AT, Ahmad J, Fagien S, Rohrich RJ. Cosmetic medicine: facial resurfacing and injectables. *Plast Reconstr Surg* 2012;129(1):142e–153e
- 25 Woodward J, Khan T, Martin J. Facial filler complications. *Facial Plast Surg Clin North Am* 2015;23(4):447–458
- 26 Rzany B, DeLorenzi C. Understanding, avoiding, and managing severe filler complications. *Plast Reconstr Surg* 2015;136(5, Suppl):196S–203S