Correcting Age-Related Changes in the Face by Use of Injectable Fillers and Neurotoxins

Mark G. Rubin, MD*, Sue Ellen Cox, MD†, Michael S. Kaminer, MD‡, and Nowell Solish, MD, FRCP(C)§

Abstract

Many patients seeking rejuvenation treatment have readily apparent age-related changes in facial features. Others exhibit more subtle changes that nonetheless can be corrected to achieve a more youthful appearance. In the following article, four specialists in aesthetic dermatology discuss how injectable hyaluronic acid–based fillers and neurotoxins can achieve rejuvenation without surgery. Semin Cutan Med Surg 33(supp4):S81-S84 © 2014 published by Frontline Medical Communications

Keywords

AbobotulinumtoxinA; aesthetic dermatology; botulinum toxin A injectables; hyaluronic acid; incobotulinumtoxinA; fillers; neurotoxins; onabotulinumtoxinA;

Effects of Aging on Midfacial and Lower Facial Appearance

The aging process changes the skin and the underlying structural support provided by the musculoskeletal system. The pace of change varies considerably from one individual to another. Moreover, tissues changes are interdependent in that age-related changes in one tissue can influence subsequent alterations in other tissues. Decreased cranial support leads to soft-tissue descent in the midface. Loss of tone in supporting musculature, increased laxity in retaining ligaments, and descent of suborbital fat pads exacerbate the downward anatomic shift. Reabsorption occurs along the mandible and maxilla, accompanied by loss of dentition. Essentially, the midface and lower face appear to collapse.

Facial Assessment

Patient satisfaction is integral to the achievement of successful cosmesis. During the facial assessment, patients should be encouraged to identify what concerns them most about the appearance of their face. That concern should become the focal point of treatment. The assessment should include the entire face, during which the clinician can identify for the patient other facial features that can be improved. However, the treatment plan should begin with the age-related change or changes that patients find most bothersome.

Use of Injectable Agents

Most patients will have several age-related facial features that can be improved with the use of injectable fillers. The areas include the temples, brow, tear trough, and midface.

Temples

Aging leads to deflation of the temple area in most patients. Diluted or reconstituted monophasic hyaluronic acid is often used to reinflate the area. Periostial placement provides a smooth cosmetic result, which is the desired outcome.

Brow

Age-related changes in the brow often can be improved by use of injectable hyaluronic acid gel. Placement of 0.5 mL of biphasic small-particle gel on both sides of the supraorbital rim elevates eyelid skin and increases brow projection.

Tear Trough

The tear trough is the depression over the medial inferior orbital rim. With aging, the fat pad descends, deepening the fold or trough in the process. One treatment option that has produced good cosmetic results in the tear trough is a newer bacteria-derived monophasic hyaluronic acid that has a uniform particle size, reduced viscosity, and greater elasticity. When injected onto the periosteum, the product fills and lifts the eyelid tissue to achieve the desired cosmetic effect. The distinct chemical structure of the product permits superficial injection without the risk of a blue discoloration known as the Tyndall effect. The biphasic small–particle hyaluronic acid product also is used frequently for this indication.

Several precautions are required when treating the periorbicular area. Many older patients are treated with anticoagulants, which should be discontinued 2 weeks before injecting a filler into the periorbicular area. Distinguishing between edema and fat pad is another consideration. If the patient gazes upward, the fat becomes more prominent, whereas edema does not. When evaluating the lower eyelid, it is important to do a lid snap test.
A poor lid snap can portend possible ectropian. Additionally, excessive tissue laxity increases the likelihood that the filler will be visible following injection. It is best to counsel patients with poor tissue elasticity to consider fractionated CO₂ to attain tissue tightening. Migration of filler over time can give a “doughy” appearance. Injections in this area require extreme caution, even for expert injectors.

**Midface**

Age-related changes involving the midface can be particularly challenging. Multiple areas often require treatment, which can involve more than one product. Midfacial filling can involve the anterior cheek, lateral malar and submalar areas, and reduction of the nasolabial area. Carefully combining the available hyaluronic acid fillers can achieve improvements that lead to subtile overall enhancement of the face.

**Randomized Trial**

The issue of age-related midface volume deficit was addressed recently in a randomized, no-treatment control group, trial. Investigators at 15 sites in North America enrolled patients who had mid-volume deficit scores ≥3 on a 6-point scale. The score was determined by evaluation of three subregions of the midface: zymatic malar, submalar, and anterior medial cheek.

Subsequently, 235 patients were treated with the volumizing hyaluronic acid filler VYC-20L, and 47 patients were allocated to no treatment. Patients in the VYC-20L group received a single treatment and an optional touch-up treatment 1 month later. Response was defined as ≥1-point improvement in midface volume deficit at 6 months. For the trial to be declared successful, 70% of patients in the treatment group had to meet response criteria. The proportion of responders had to demonstrate statistical superiority over the control group.

When the trial ended, the results showed that 85.6% of patients in the treatment group were responders compared with 38.9% of the control group (P<0.001). Analysis of different categories of response showed consistent superiority for the treatment group for the proportion of patients who improved by ≥1.5 (71% vs 17%, P<0.001), ≥2.0 (51% vs 11%, P<0.001), and ≥2.5 (26% vs 0%, P<0.001). After 2 years of follow-up, 67.1% of patients in the treatment group met response criteria. Patient satisfaction with improvement was 89.8% at 6 months and 75.8% at 24 months.

**Aging and the Lower Face**

Many of aging’s effects on the lower face involve loss of structural support, leading to loss of volume and an overall descent of facial features. Surgery can restore a more youthful appearance by lifting and correcting the tissue descent. Nonetheless, judicious use of fillers can aid in restoring a more youthful appearance to the lower third of the face. Areas that can benefit from fillers include oral commissures, perioral lines, marionette lines, prejowl and postjowl sulcus, and chin enhancement.

**Focus on Fine Lines**

Development of fine lines in the perioral area is a common consequence of aging in the skin. Injectable collagen once formed the basis of treatment for fine lines. When collagen was withdrawn from the market, dermatologists evaluated various dilution strategies with hyaluronic acid, which led to inconsistent results.

A newer polydensified hyaluronic acid gel filler has proven useful as an alternative to diluted hyaluronic acid products, providing more consistent results. A recent review of safety and efficacy trials showed that the gel filler achieved durable results that were noninferior and superior to bovine collagen. A comparison with two other hyaluronic acid compounds demonstrated similar and generally favorable safety profiles, and a 5-year retrospective study of the gel filler revealed no severe adverse events, including no persistent nodules or granulomas.

Unlike other hyaluronic acid fillers, the gel compound has no anesthetic, making injections more painful. The product can be diluted with lidocaine before administration to reduce the pain. Dilutions of the gel with the addition of variable amounts of 1% lidocaine can be used to treat age-related lines, adjusting the dilution to achieve the desired amount of lift or inflation in a line. In most cases, treatment of fine lines with 1 cc of the hyaluronic acid gel diluted with 5 cc of 1% lidocaine provides durable results, lasting 4 to 5 months or longer before requiring additional correction.

**Neurotoxins and Neuromodulators**

Clinicians and patients can choose from three neurotoxins or neuromodulators that have approval from the US Food and Drug Administration: onabotulinumtoxinA, abobotulinumtoxinA, and incobotulinumtoxinA. All three products can achieve favorable aesthetic results when applied to age-related changes in the lower face. However, clinicians and patients may favor one product over the others because of clinical experience or subjective factors.

**Challenges of Treating the Lower Face**

The lower face offers multiple potential targets for aesthetic application of neurotoxins. Facial musculature is layered, and treating one muscle without affecting an underlying or underlying muscle requires precise, careful injection of a neurotoxin. Unlike muscles of the glabellar complex, muscles of the lower face have functional roles that can be adversely affected by imprecise placement of a neurotoxin.

Clinicians often have a small margin of safety for achieving desired aesthetic results without weakening functionally important muscles by unintentional exposure to a neurotoxin. The products should be used in these areas only by experienced clinicians.

**Principles of Aesthetic Application of Neurotoxins**

Regardless of the target for injection, careful examination of the muscle tone, strength, and symmetry, as well as the potential efficacy, is essential. In all cases, treatment should begin with the lowest possible dose of a neurotoxin. If a dose does not achieve the desired aesthetic result, additional product can be administered. This conservative approach is the safest way to proceed in these areas because the effects of overtreatment are irreversible until the neurotoxin wears off over the course of several months.

**Common Lower-Face Applications**

**Nefertiti Lift**

Named for the distinct jawline of the ancient Egyptian queen, Nefertiti injections of a neurotoxin are designed to decrease the downward pull of the platysma on the lower cheek. The aesthetic goal is to raise the jawline and reduce the jowl.
Nefertiti injections are among the simplest procedures involving neurotoxins, and complications are uncommon. A similar effect can sometimes be achieved with a volumizing filler in the midface, but a neurotoxin may offer a more efficient, less costly means to reduce jowls and improve the jawline on the lower face. Injecting a neurotoxin into the platysmal band can correct some age-related neck bands but will have little effect on skin laxity and redundancy in the neck.

**Marionette Lines**
Another common dermatologic manifestation of aging is the appearance of downward-turning oral commissures and curved wrinkles in the marionette area. Targeting the depressor anguli oris (DAO) muscle for neurotoxin injection can help reduce these changes. Precise injection of the neurotoxin into the DAO is essential. The DAO can be distinguished from the depressor labii by palpation of the former. The muscle also can be identified by asking patients to clench their teeth and injecting just medial to the anterior edge of the clenched masseter muscle.

In most patients, both sides of the mouth should be treated. Some patients have asymmetrical DAO musculature, in which case different doses may be needed for each side. In some cases, only one side needs to be treated.

**Cobblestone Chin**
Many patients have never noticed this effect until it has been brought to their attention. Tissue atrophy can result in a rippled or nodular appearance in the chin. The effect tends to be subtle or unnoticeable when the chin is relaxed. Facial animation, such as during a conversation, can reveal changes, which are most noticeable to observers, not the patient. The effect can be most easily observed by the patient with contraction of the mentalis muscle. The nodular or dimpling appearance can be corrected by injecting a neurotoxin into the mentalis muscle.

**Perioral Wrinkles**
Correcting perioral wrinkles requires treatment of the orbicularis oris. The challenge is to administer a neurotoxin dose that relaxes the muscle sufficiently to reduce wrinkling without creating problems in the lips, including when pursing, whistling, speaking, and perhaps even eating. Combining a small dose of neurotoxin with a filler often provides the best aesthetic results with less risk of causing the previously mentioned problems in the lips from too much neurotoxin.

Treating numerous small wrinkles above the upper lip with a neurotoxin is more difficult than correcting a few large muscle-related wrinkles. Patients with numerous small wrinkles may require a degree of correction greater than what can be expected with a neurotoxin and filler. These patients may need laser resurfacing to achieve an optimal result.

Wrinkles below the lower lip require more precise treatment and carry a substantial risk of complications related to incorrect placement of injections or an excessive dose of neurotoxin. Because the doses need to be very low in this area, neurotoxins are less effective in correcting lines radiating downward from the lower lip, and the risks might outweigh the potential benefits in many cases.

**Masseter Injections**
Injecting a neurotoxin into the masseter can reduce facial width, and treatment is sought more often by Asian patients than by Caucasian patients. To achieve the thinning effect, a clinician will usually inject 15 to 20 units of neurotoxin product on each side of the face, and an injection depth of ¼ to ½ inch is required. Caucasian patients who seek masseter injections often clench their teeth on a regular basis, resulting in muscular hypertrophy that can be improved by treatment with a neurotoxin.

**Excessive Gum Exposure**
Excessive exposure of the gums when smiling is indicative of hyperfunctional levator labii superioris alaeque nasi. Quite often, a single small-dose injection below and to the side of each nare can achieve the desired lowering of the upper lip with a concomitant reduction in gum exposure.

**Tear Trough Fillers**
Multiple hyaluronic acid–based fillers, used in a variety of dilution concentrations, can achieve the desired aesthetic improvement in tear troughs, the areas immediately below the lower eyelids. Although all of the available products can produce good results, the products have subtle differences in structure, consistency, and other parameters that may make one product superior to another for specific indications. To achieve the best results on a consistent basis, clinicians should determine which product is optimal for a specific technique or application and then use that product consistently for the indication.

**Product Choice and Dilution**
During the process of accumulating experience with specific filler products, clinicians can determine the strengths and limitations of different fillers. They might find that certain gel fillers are less likely to produce the Tyndall effect. The consistency of a product might be too dense or too thin for a specific aesthetic application. Recognition of these subtle differences comes primarily from experience in using them.

Dilution can improve the flow characteristics of fillers when used in the tear trough, and injection-site discomfort will differ depending on anesthetic content of the dilution. No single dilution formula can be applied to all fillers or to all of the applications for which fillers are used.

**Injection Site**
The choice of injection site is a key decision in the use of injectable fillers to treat hollow tear troughs. One option is to inject along the periosteum of the orbital rim, where care has to be taken to avoid injecting the orbital septum. Most anatomic drawings show the orbital septum attached to the apex of the orbital rim. However, anatomic variance can result in the insertion of the septum several millimeters inferior to the orbital rim. Inadvertent injection of the orbital septum can lead to injection of filler into the orbital fat, as well as small tears in the septum itself.

An alternative approach to injecting the tear troughs is the “potential space” technique, which requires precise injection of filler into a narrow plane deep to the orbicularis oculi muscle and superficial to the periosteum. The technique involves needle penetration deep to the orbicularis oculi muscle, usually in the mid-papillary line to start. Most injections begin a few millimeters inferior to the orbital rim. Approximately 0.2 to 0.4 cc of filler material is placed in the potential space deep to the orbicularis oculi muscle and then gently pushed or massaged medially to fill the medial tear trough adjacent to the medial canthus. Additional injection points can be added medial to the
initial site, taking care to avoid touching the periosteum with the needle. A similar technique can be used to fill the lateral tear trough, using this potential space approach.

The primary advantages of the potential space technique are avoidance of the orbital septum; fewer needle puncture sites, which can reduce trauma and bruising; and ability to mold filler in the potential space to achieve smooth contours.

**Combining Techniques for Maximal Aesthetic Efficacy**

Although no two patients are alike, they share the common goal of achieving a specific aesthetic effect. In some cases, the goal can be met with a single procedure. In other cases, a combination of procedures and techniques might be required to attain the patient’s aesthetic goal.

**Focus on the Patient**

Focusing on the patient begins with an overall assessment of the patient’s face: extent and location of volume loss, types of aesthetic improvements that can be achieved, and techniques and materials that will be required to achieve the optimal aesthetic effect for the individual patient.

The facial assessment should include examining the changes that have occurred with aging: specifically, volume loss and redistribution associated with facial fat and muscle and bony changes that occur with aging. Replacing volume where needed will help reverse the appearance of the patient’s specific aging pattern. Additionally, reallocating volume and using toxin to help shape the patient will achieve an even better overall result. Some treatments can help give the patient better proportions and balance. This may not make the patient look more youthful, but it will make the patient’s overall appearance more cosmetically pleasing.

A comprehensive treatment plan should include consideration of which fat pads can be treated to achieve the optimal effect, which techniques will be required, and which materials will be needed.

The overall assessment should comprise the upper face, midface, and lower face.

**Upper Face Forehead**

The assessment should begin with identification of changes involving bone, fat, and skin. Mapping the patient’s face by drawing on the skin can aid in achieving the desired aesthetic effect and, at the same time, avoid structures and tissues that lead to complications if injured. One must assess the projection of the forehead. If the patient has poor projection of the forehead, it can contribute to the downward displacement of the brow and more horizontal lines on the forehead. When placing volume in this area of the forehead, it is prudent to know the position of the supratrochlear and supraorbital arteries. In addition to properly placed toxin, this volume replacement will result in elevation of the brow, diminution of the forehead lines, and a much more youthful appearance.

Injection of a volume-enhancing filler in this area can achieve excellent results that also are very long lasting.

**Midface**

Assessment of the midfacial area begins with the cheek, lower lid, and submalar area. The severity of age-related laxity in these areas can determine whether a patient can be treated with fillers or will require surgery. For many patients, nonsurgical treatment can achieve the desired youth-restoring effects.

From the cheek, the assessment progresses to the junction between the lower eyelid and the cheek, the lid-cheek junction. I first add volume to the cheek to diminish the lid-cheek junction, and usually less volume is required to correct any remaining tear trough deformity. Limited treatment of this area and the midcheek often has a substantial rejuvenatory effect.

The submalar area is another common site for filler injection. This area is harder to treat as there is no bony support underneath on which to place the product. Depot or fan-technique injections can add volume that complements the midcheek treatment. Loss of volume in the submalar area is common among younger, athletic women who are well toned and have low levels of body fat. The same changes can be observed in athletic men but are more commonly seen in women.

**Lower Face**

The lower face often has multiple age-related changes that can be improved by use of injectable fillers. Marionette lines, loss of chin projection, and loss of volume in the mandibular area are common age-related changes that can be corrected. Some patients find sagging jowls particularly bothersome. Judicious use of a neurotoxin and filler can achieve a lifting effect that reduces or eliminates the facial descent in the jowl area, resulting in a better-toned, more youthful appearance.

**References**

3. Cox SE, Murphy DK, Paradkar D, Few JW. Subject-reported outcomes over 2 years with a volumizing hyaluronic acid filler for mid-face volume deficit. In Press.