Contemporary Techniques and Controversies in Nonsurgical Rejuvenation of the Eye

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The eyes are a focal point of facial beauty and manifest some of the most telltale signs of facial aging. As more patients are opting to defer or forgo surgical intervention such as blepharoplasty, the dermatologist has the potential to be at the forefront of periorbital rejuvenation. Periorbital aging involves all layers of the skin, fat, and even the bony orbit, and as such, the periorbital complex presents unique anatomic and aesthetic challenges that must be considered. We review contemporary nonsurgical approaches to rejuvenation of the eye with attention to pertinent anatomy, proper patient selection, variations in technique, and potential complications. Modalities such as neurotoxins, fillers, lasers, radiofrequency (RF) devices, ultrasound technology, chemical peels, and topical therapies are reviewed in the context of periorbital rejuvenation.

The eyes are the cornerstone of facial beauty and a unique feature that defines us as individuals. With the ability to both take in external stimuli and project internal emotion, our life is reflected in our eyes. Anatomic challenges must be considered in a comprehensive strategy for periorbital rejuvenation, and aging affects the eye at all levels from the bony orbit to the epidermis. Some of the most common chief concerns of patients seeking cosmetic evaluation involve the eye and periorbital complex. From dark circles to crow's-feet, a plethora of products and devices are available to physicians to address these issues and obtain favorable results. It is important for the patient and physician to understand the types of defects that can be improved using noninvasive techniques and those that require a surgical approach. In this article, we review contemporary nonsurgical approaches to rejuvenation of the eye with attention to pertinent anatomy, proper patient selection, variations in technique, and potential complications.

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NEUROTOXINS AND EYE REJUVENATION

Crow's-feet

One of the telltale signs of aging in the periorbital region is the development of the radial wrinkles known as crow's-feet. They are formed primarily from the repeated contraction of the orbital portion of the orbicularis oculi muscle with some contribution from the zygomatic muscles in the formation of infraorbital lines. OnabotulinumtoxinA (Botox Cosmetic, Allergan, Inc) was first

approved for cosmetic indications in 2002 and currently carries US Food and Drug Administration (FDA) approval for the treatment of glabellar rhytides. Since 2002, the safety and reliability of botulinum toxin has led to its use in a myriad of off-label indications including the treatment of periorbital rhytides.

Crow's-feet can be effectively treated using 2 to 4 U of botulinum toxin at each of 3 or 4 injection sites per side. The consensus regarding the distance from the orbital rim for placement of these injections has changed somewhat over the last 5 years. It was initially thought that they must be placed at least 1.5 cm lateral to the orbital rim to minimize the risk for diffusion of toxin into the motor muscles of the eye. The 2010 multidisciplinary French consensus on the treatment of upper and midface aging using onabotulinumtoxinA, however, recommends a safety margin of only 4 to 5 mm from the orbital ridge, with injections placed above the inferior margin of the zygomatic arch.[1] There are other injectors, however, who still advocate a safety margin of at least 1.5 cm from the ridge. The injection technique for crow's-feet entails superficial (up to the first one-third of the needle) hypodermic injections at an angle of 20° to 30° to the skin with care to avoid the dense network of superficial vessels in this area.[2] Care also must be taken to keep the injection site above the zygomatic arch to avoid paralyzing the zygomaticus major muscle that elevates the upper lip. Inadvertent injection into this muscle results in the inability to lift the ipsilateral upper lip and a crooked smile. Treatment of crow's-feet with botulinum toxin has the added benefit of weakening the lateral eyebrow depressors, resulting in a lift of the lateral tail of the eyebrow.

Lower Eyelid Lines

Lower eyelid lines are caused by the repeated contraction of the palpebral portion of the orbicularis oculi muscle. These lines are more difficult to eradicate than crow's-feet, requiring a more conservative approach to avoid disturbances in blinking as well as the development of lower eyelid sagging and scleral show. One of the more novel off-label uses for botulinum toxin in the lower eyelid is to widen the palpebral aperture in patients with a hypertrophic orbicularis oculi muscle. Such hypertrophy leads to a puffiness or "jelly roll" under the eye at rest and a reduction in the palpebral aperture when smiling. The injection technique calls for 1 to 2 U (no more than 2 U) placed 3 mm below the lower eyelid margin in the midpupillary line.[3] Asking the patient to look upward can facilitate the injection, which should be positioned parallel to the eyelid border and placed intradermally.[1] An adequate assessment of lower lid laxity using the snap test is particularly critical when considering infraorbital injections, and patients with any hint of lower lid laxity should not be considered appropriate candidates. Additionally, repeated injection into the lower orbicularis oculi, even at low volumes, introduces the risk for eventual atrophy and weakening of the muscle. This weakness eventually can lead to herniation of the infraorbital fat-pad and worsening of periorbital hollowness and dark circles. Because herniation of the fat-pad can only be addressed surgically, many injectors have abandoned lower lid toxin injections in the treatment of infraorbital rhytides in favor of other modalities.

Brow Shaping

The position of the brows has a remarkable impact on the overall aesthetic of the periorbital region. Brow ptosis can make the eyes appear smaller, and dropping of the lateral tail of the brow renders a tired or sad appearance. Treatment of crow's-feet often will produce a secondary effect of lifting the lateral brow. The lateral brow also can be specifically targeted to afford an additional lift. The frontalis muscle lifts the brow and is in opposition to the corrugator, procerus, and orbicularis oculi muscles, which pull the brow down. The orbicularis oculi pulls the lateral brow down, whereas the corrugator and procerus muscles depress the medial brow. Injecting 2 to 7 U of botulinum toxin type A at each eyebrow tail in the superior and lateral aspects of the orbicularis oculi muscle can achieve the desired lateral lift and function as a temporary brow-pexy effect. The injection should be perpendicular to the skin, intramuscular, and to the middle third of the needle.[2] Injections of 7 to 10 U of botulinum toxin type A to each lateral orbicularis oculi yield an average brow elevation of 1.02 mm from the mid pupil and 4.83 mm from the lateral canthus that is maintained for 3 to 4 months.[4]

FILLERS: THE TEAR TROUGH AND THE UPPER ORBIT

The tear trough, or nasojugal groove, extends inferolaterally from the medial canthus at the border of the eyelid and the cheek and is bounded superiorly by the infraorbital fat protuberance and inferiorly by the upper cheek, the suborbicularis oculi fat, and part of the malar fat-pad.[5] Even in young people, there is variation in the depth of the tear trough, but the effects of aging, including atrophy of the skin, soft tissue, and bone, contribute to deepening of the trough and an appearance of looking perpetually tired.

Restoring volume to the tear trough with hyaluronic acid (HA) may allow some patients to achieve a more youthful eye without having to undergo surgery. Tear

trough injections are notoriously tricky, even for the most experienced injectors. Physicians must be cautious to avoid vascular structures and to place the filler at the correct level to avoid contour defects, bruising, and the Tyndall effect. There is no single gold standard method for tear trough injections, and many injectors use different techniques with equal, cosmetically acceptable results. In the serial puncture technique, aliquots of 0.1 mL of HA are placed in a preperiosteal plane immediately inferior to the orbital rim and then molded superiorly into the tear trough. In a retrospective study of 25 patients treated with HA in the tear trough using a serial puncture technique, the average volume needed to achieve correction was 0.5 to 0.6 mL per side, and the most common complication was bruising seen in 52% (13/25) of patients.[5] Other tear trough injection techniques include placing threads of filler beneath the orbicularis oculi muscle or placing filler both in the muscle and at the periosteum.

Hyaluronic acid fillers also can be used to treat volume loss of the upper eyelid and orbit. Although many patients develop excess upper eyelid tissue with associated ptosis and hooding, there is a subset of patients, often younger, who have atrophy of upper eyelid tissue. The standard treatment for adding volume to the upper orbit has long been fat grafting, which is an invasive surgical procedure, but it may be possible to obtain similar results using HA fillers. Liew and Nguyen[6] described the results of a series of 36 patients treated with HA to restore volume to the upper periorbital area. Injector technique involved topical anesthesia to the upper eyelid for 20 minutes followed by aliquot injections of 0.1 mL of product inserted at a 30° angle to the skin along the upper periorbital rim at the supraperiosteal level. The product was then massaged inferiorly into the junction between the lower brow and the upper eyelid. The average volume of filler ranged from 0.2 to 0.6 mL per orbit, and the reported duration of effect was as long as 3.5 years. The authors recognized the potential for adverse events when injecting in the upper orbit, including intravascular injection, supratrochlear and supraorbital nerve injury, and embolization of product. They recommended that the technique be limited to practitioners with substantial experience and in-depth knowledge of the anatomy.[6]

LASERS AND PERIORBITAL REJUVENATION

Laxity and wrinkling of the upper eyelids is a common manifestation of facial aging. The delicate nature of the eyelid skin and its proximity to the globe makes this region particularly challenging to treat. The CO_2 laser (10,600 nm) targets water as its chromophore, vaporizing the entire epidermis and a variable thickness of the dermis. With the advent of fractional photothermolysis, it became possible to harness the power of the CO_2 laser in small microthermal zones of injury that leave intervening skin normal, thus minimizing tissue damage and hastening the reepithelialization process. Fractional CO_2 lasers have been used to treat both upper and lower eyelid laxity with good cosmetic results. Metal shields must be inserted to protect the eyes. A recent study described a cohort of 45 patients with Fitzpatrick skin types I and II who received 2 or 3 treatments with a fractional CO_2 laser to the upper and lower eyelids and periorbital region.[7] One year after treatment, the largest percentage of patients treated (33% [15/45]) had a global improvement score of moderate improvement for eyelid tightening, texture, and periorbital fine lines on a scale that measured slight, moderate, marked, and excellent improvement. The vast majority of patients (60% [27/45]) reported being very satisfied with the degree of improvement in periorbital skin tightening and wrinkle reduction. Adverse events were minimal and included swelling, redness, and long-standing erythema in 3 patients that persisted for as long as 28 days.[7]

For patients with minimal rhytides or for those who cannot tolerate any postprocedure downtime, nonablative fractional resurfacing may provide some degree of improvement. Patients should be advised that the results are less dramatic than those obtained with ablative resurfacing and multiple treatments may be required. In a study of 31 patients with upper eyelid laxity and rhytides treated with a 1550-nm erbium-doped fiber laser, all patients obtained some degree of eyelid tightening, and 55.9% (mean of 21/31, 15/31, and 16/31) had an increase in eyelid aperture. However, because the eyelids were treated in conjunction with the entire face in this study, it is unclear if treating the eyelids alone would yield similar results.[8]

RADIOFREQUENCY DEVICES

Radiofrequency (RF) generates an electric current that produces heat in the dermis and subcutaneous tissue without damage to the overlying epidermis. The skin-tightening effect of RF is believed to result from immediate contraction of collagen fibrils that denature when heating with subsequent neocollagenesis as part of a long-term, wound-healing process that occurs over several months.[9]

Two commonly used RF devices include Thermage (Solta Medical) and Pellevé (Ellman International, Inc), with Pellevé delivering continuous RF in contrast to Thermage, which delivers pulsed RF. Some argue that continuous RF allows for a safer, more controlled delivery of RF, though there are no randomized controlled studies

comparing the 2 devices. Thermage is a 6-MHz monopolar RF device that is FDA approved for the treatment of periorbital rhytides and wrinkles including the eyelids as well as temporary improvement of cellulite. A special, shallow, 0.25-cm^2 treatment tip that heats to a depth of only 1.2 mm beneath the skin was developed specifically for the eyelids. The results of a 2006 prospective multicenter trial of 72 patients treated with monopolar RF for eyelid laxity demonstrated tightening of the upper lid in 88% (63/72) of treated patients, with 71% (51/72) to 74% (53/72) noting lower lid tightening. Most patients obtained at least 25% improvement, with a smaller fraction obtaining better results.[10]

Pellevé can deliver monopolar or bipolar RF depending on the handpiece used and is FDA approved for the treatment of mild to moderate facial wrinkles and rhytides in Fitzpatrick skin types I to IV. In contrast to Thermage, treatment with Pellevé does not require anesthesia or external cooling of the skin. A treatment gel ensures proper coupling of the device, and the Pellevé electrodes are moved in a circular pattern over the skin with 3 to 4 passes that raise the skin temperature to 42°C.[11,12] A study of 32 patients treated with a 4-MHz RF device similar to Pellevé (Surgitron Dual RF S5 device, Ellman International, Inc) for periorbital rhytides and midface laxity noted appreciable, albeit modest, results.[11] At 6 months posttreatment, 46.9% (15/32) of patients reported minimal improvement, 43.8% (14/32) noted mild improvement, and only 9.4% (3/32) noted moderate improvement during self-evaluation. The eyelids were not included in the treatment area, and the authors specifically advocated extreme caution and the need for further study regarding proper settings and safety parameters in this region.[12]

INTENSE FOCUSED ULTRASOUND

Intense focused ultrasound (IFUS) works via acoustic energy that creates friction between molecules and leads to the generation of heat and focal tissue damage.[13] Ultrasound energy has been used for several years in the treatment of benign and malignant tumors of the prostate. More recently, the technology has been refined and adapted for more focal applications at much lower energies. The Ulthera System (Ulthera, Inc) was FDA approved in 2009 for nonsurgical brow-lifting and thus has the potential to enhance the overall aesthetic of the periorbital region, especially when combined with fillers or neurotoxins.

Intense focused ultrasound creates inverted conical-shaped zones of thermal coagulation of approximately 1 mm^3 with a depth of penetration of up to 4.5 mm beneath the skin depending on the settings used. In contrast to lasers, ultrasound devices are capable of selectively delivering energy to the subcutis, sparing the overlying dermis and epidermis. A 2010 study evaluated the efficacy of IFUS skin tightening in treating the upper face in the context of full-face and neck treatment.[13] The study was a rater-blinded prospective cohort study of 35 patients treated with IFUS to the forehead, temples, cheeks, submental region, and sides of the neck. Three blinded reviewers were asked to identify the pretreatment and posttreatment (90 days) photographs with the procedure considered successful if the photographs were correctly identified, a failure if they were incorrectly identified (eg, a photograph was identified as posttreatment when it actually was pretreatment), or no change if there was no appreciable difference. Brow position was similarly evaluated using pretreatment and posttreatment photographs, with 86% (30/35) of participants showing appreciable brow-lift as assessed by 3 blinded evaluators ($P=.00001$) with a mean change in brow height of 1.9 mm.[13] Thus the combination of tightening procedures that lift the brow superiorly with resurfacing of the eyelid skin has the potential to provide multidimensional improvement to the periorbital region.

TOPICAL THERAPY FOR EYELASHES

The eyelashes serve a physiologic purpose to protect the eyes and are key components of the aesthetically ideal eye. Similar to scalp hair, eyelashes are terminal hairs, but they have several unique biologic properties that differentiate them from scalp hair. Eyelashes are thicker than scalp hair, do not grey with age, and are not influenced by androgens.[14]

Bimatoprost ophthalmic solution 0.03% was approved by the FDA in 2008 for the treatment of eyelash hypotrichosis. A synthetic prostaglandin analog used for more than 10 years to treat glaucoma, it was serendipitously noted to have the side effect of eyelash hypertrichosis in 42.6% of patients using daily bimatoprost for 1 year.[15] The mechanism of action of bimatoprost is 3-fold: it increases the percentage of lash follicles in the anagen growth phase; stimulates melanogenesis, resulting in darker lashes; and increases the size of the dermal papilla and hair bulb.[16] The safety and efficacy of bimatoprost solution 0.03% was evaluated in a large, industry-sponsored, multicenter, randomized, double-masked, vehicle-controlled study of 137 patients treated with active drug and 141 patients treated with empty vehicle.[17] Digital image analysis software was used to assess the length, thickness, and darkness of the eyelashes at 4-week time intervals. Statistically significant longer length was noted in the bimatoprost group versus the control group as early as 4 weeks and was maintained until the end of the study at 20 weeks ($P<.001$). The

only adverse event that occurred significantly more frequently in the treatment group than in the control group was conjunctival hyperemia ($P=.03$), which occurred in 3.6% (5/137) of participants. There were no cases of iris hyperpigmentation, which is of particular concern for many patients who are considering bimatoprost for a cosmetic indication.[17]

It is important to counsel patients that cases of iris hyperpigmentation were reported when bimatoprost was used as an eyedrop to treat glaucoma as well as in a few postmarketing cases when used for hypotrichosis.[14,18] Bimatoprost solution 0.03% is applied only to the skin of the upper eyelid, and the dose applied is only 5% of that used to treat glaucoma; thus when the solution is applied as directed, the risk for hyperpigmentation is very low. However, because the hyperpigmentation is considered to be irreversible, it should be discussed with patients prior to starting use of bimatoprost.

CHEMICAL PEELS, TOPICAL AGENTS, AND OTHER CONSIDERATIONS

With age, the skin of the upper eyelid atrophies and becomes loose and redundant as the connection to the underlying muscle is compromised. This tissue laxity, termed *dermatochalasis,* is best repaired by surgically removing the excessive tissue via blepharoplasty. For patients with minimal laxity or those unwilling to accept the risks of surgery, other strategies such as chemical peeling have been employed. Trichloroacetic acid is a commonly employed agent in blepharopeeling, and histologic studies of postpeel eyelid skin show that 2 applications of trichloroacetic acid (ranging from 20%–50% in concentration) without prior retinoic acid application is unlikely to produce a degree of dermal injury that could cause contraction or ectropion.[19] One pilot study of 8 patients described the application of a Baker-Gordon phenol peel to the upper eyelid skin fold in conjunction with 88% phenol in the remaining periorbital region.[20] Patients had preprocedure laboratory tests, electrocardiograms, and eye examinations and were given a week of antiviral prophylaxis starting 2 days prior to the procedure. The healing time for the eyelid was 6 to 8 days, after which the authors reported improvement in upper lid laxity and fewer periorbital rhytides with no major adverse events. They advised that the application of the Baker-Gordon peel should be restricted to the area of skin excess and not the entire eyelid in patients with Fitzpatrick skin types I to III.[20]

Topical agents can be used in conjunction with other modalities. Although topical retinoids remain the gold standard for photoaging, many patients are unable to tolerate them around the eye. A comprehensive review of cosmeceuticals marketed for the eye is beyond the scope of this review, but there are trends that practitioners should note. One such trend is the development of natural antioxidants such as niacinamide. Antioxidants are the largest category of cosmeceutical ingredients incorporated into topical treatments and will likely remain so for the next several years.[21] They can be divided into 3 main categories: carotenoids, flavonoids, and polyphenols. The carotenoids are derivatives of vitamin A and thus are components of many cosmeceuticals because of their similarity to retinoids. The flavonoids are aromatic compounds with antioxidant and UV-protection properties. Commonly used flavonoids in cosmeceuticals include soy, milk thistle extract, and ginkgo. The polyphenols represent a subset of flavonoids and include common cosmeceutical ingredients such as green tea, pomegranate, and grape seed extract.

An assessment of any cosmetic patient should include a smoking history, as the periorbital and perioral regions are particularly vulnerable to the deleterious effects of cigarette smoke. A recent study demonstrated that after only 30 minutes of cigarette smoking, there was a significant ($P<.001$) increase in temperature accompanied by a significant ($P=.02$) decrease in the oxygenated hemoglobin content in the periocular skin.[22] The hypoxic state of skin induced by cigarette smoking has a negative impact on cell metabolism. Thus the investment of thousands of dollars in cosmetic modalities for periorbital rejuvenation may prove futile in a patient who is an active smoker. The cosmetic dermatologist in turn has the potential to alter a patient's overall health and life expectancy by encouraging smoking cessation, even if for purely cosmetic reasons, as physical appearance and the desire to maintain youth can be powerful motivators in many patients.

CONCLUSION

As more cosmetic patients are opting to defer or avoid surgery in favor of noninvasive modalities, the dermatologist has the potential to be at the forefront of periorbital rejuvenation. Neurotoxins, fillers, lasers, RF devices, chemical peels, and cosmeceuticals can all be used as part of a global strategy to address the dimensions of the aging eye. Proper patient selection and management of expectations are critical to the success of any cosmetic intervention. Although we have many new tools and tricks to combat aging, it is important not to forget basic patient education about skin care including protection from UV light and cessation of smoking.

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