The Role of Injectable Devices in Nonsurgical Facial Rejuvenation: Clinical Impressions and Recommendations

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Citation

B Azizzadeh. *The Role of Injectable Devices in Nonsurgical Facial Rejuvenation: Clinical Impressions and Recommendations*. The Internet Journal of Aesthetic and Antiaging Medicine. 2009 Volume 2 Number 2.

Abstract

Noninvasive and minimally invasive, nonsurgical facial soft-tissue augmentation procedures are becoming increasingly popular alternatives to traditional rhytidectomy. As the processes underlying facial aging are elucidated, new techniques addressing facial volume loss will be required. Nonsurgical face-lifts utilize combinations of injectable agents and devices, including botulinum toxin type A, hyaluronic acid derivatives, poly-L-lactic acid, and calcium hydroxylapatite. The agents chosen by the clinician depend on the type of defect and the facial area involved. Botulinum toxin type A is the most commonly used product in the correction of dynamic rhytides, whereas injectable devices are used to correct depressions in the nasolabial fold, orbital rim, cheeks, and oral commissure. This article will review the various devices available and provide insights gained during the author's own clinical experience with nonsurgical facial soft-tissue augmentation.

ABBREVIATIONS

FDA = US Food and Drug Administration
HIV = human immunodeficiency virus
Nd:YAG = neodymium:yttrium-aluminum-garnet
PLLA = poly-L-lactic acid

INTRODUCTION

Over the previous 10 years, there has been a 754% increase in the number of cosmetic procedures performed in the United States.[1] Of the 11.7 million procedures performed in 2007, 82% were nonsurgical and commonly involved facial volume replacement[1]; expenditures for these cosmetic procedures totaled nearly $13.2 billion,[1] compared with $12.4 billion in 2005.[2] This suggests that there is an increase in individuals' search for ways to maintain a youthful appearance without undergoing surgery.[3]

The processes underlying the characteristic appearance of the aging face are primarily related to soft-tissue changes, such as volume loss and skin laxity, although bone remodeling also plays a role.[4-6] Facial volume loss is the result of age-related atrophy of subcutaneous adipose tissue, overall thinning of the dermis due to a reduction in the glycosaminoglycan and proteoglycan content, and bone atrophy and remodeling.[6,7] In addition, downward shifts in facial fat position with age and the effect of gravity result in a loss of fullness in the malar region and lateral cheek and the elongation of the face.[8] Furthermore, as an individual ages, dermal elastosis results in a decrease in the tautness of the skin, which in conjunction with dermal thinning, contributes to the formation of static rhytides.[5,6,9] Dynamic expression rhytides represent the cumulative effects of repeated contraction of facial muscles over time.[7,9] Although it is generally believed that age-related relaxation of facial muscles[6] contributes to the development of rhytides, the improvement in the appearance of rhytides following botulinum toxin injection and the results of magnetic resonance imaging studies of facial soft tissue do not appear to support this hypothesis.[6,10]

A detailed discussion of rhytidectomy is beyond the scope of this paper; however, Stuzin[8] provided an extensive review of surgical face-lift procedures. Briefly, rhytidectomy remains the gold standard for correcting moderate to advanced lower facial and neck laxity and age-related changes. For individuals with advanced facial aging, rhytidectomy in combination with fat grafting and/or facial implants is the best option. Nevertheless, many patients may not be appropriate candidates for this technique because of the inherent risks associated with surgical procedures or the patient's desire to avoid invasive procedures. This is particularly true for elderly patients and individuals with concomitant medical conditions; thus, careful preoperative screening is required.[8] In my own practice, I find that many

patients are not prepared to undergo surgery and seek a less invasive approach. In these cases, injectable facial rejuvenation is an acceptable alternative.

The term "liquid face-lift" has been used extensively in online advertisements to describe minimally invasive, nonsurgical approaches to facial rejuvenation utilizing injectable devices. Approaches include the use of combinations of devices based on the needs of the individual patient. Nonsurgical facial rejuvenation satisfies the need that some patients have for a rapid procedure (usually takes less than 1 hour to perform) that is associated with a lower risk of complications than surgery and which produces effects that are long-acting. The full effects of some nonsurgical face-lifts may take time to develop, which is preferred by patients who do not wish to see a dramatic change in appearance. This approach is prevalent in aesthetic clinical practices, but the actual procedures and products used vary from practice to practice.

There is no consensus on the best technique to use when measuring facial atrophy that is the result of aging, trauma, or disease. As a result, the aesthetic clinician is immediately presented with a number of challenges when choosing the most appropriate procedure for each patient.[5] It is difficult to compare data from different clinical studies that have used diverse methods for assessing lipoatrophy, and it is challenging to accurately assess the benefits of treatment in clinical practice in the absence of a standardized assessment method. Thus, the evaluation of treatment candidates becomes subjective and open to criticism. Therefore, selection of the method of cosmetic intervention (surgical vs nonsurgical) must be based on an examination of the patient and an analysis of the face in its entirety (ie, brow and forehead area, eyelids, cheeks and mid face region, and lower face and neck). Only then, following a thorough discussion with the patient regarding the advantages and disadvantages of each type of treatment, can a treatment strategy be formulated.

The purpose of this review is to discuss the role of injectable agents, including botulinum toxin type A, hyaluronic acid derivatives, calcium hydroxylapatite, porcine collagen gel, and poly-L-lactic acid (PLLA) (Table) in minimally invasive cosmetic procedures and techniques. In addition, I will share insights gleaned from my own clinical experience with the use of injectable devices in nonsurgical face-lifts. Bovine- or human-derived collagen products are not included in this discussion, because I do not use them in my own practice, and I believe their overall use is declining, primarily because of their short duration of action. A porcine-derived collagen gel (dermicol-P35; Evolence) was recently approved by the US Food and Drug Administration (FDA) for the correction of moderate to deep facial wrinkles and folds such as nasolabial folds; the duration of action is up to 18 months.[11-13] I have limited experience with this product, but it appears to offer another potential alternative in soft-tissue augmentation.

APPROACHES TO NONSURGICAL FACE-LIFTS

A survey of board-certified plastic surgeons, dermatologists, facial plastic surgeons, and otolaryngologists revealed that almost 2.8 million of the 9.6 million nonsurgical cosmetic procedures performed in 2007 involved botulinum toxin type A injection and 1.7 million procedures involved the use of autologous fat, calcium hydroxylapatite, collagen, hyaluronic acid products, injectable PLLA, or polymethyl methacrylate in collagen.[1] The facial area and type of deformity and/or defect involved determines which agent is most appropriate.

BROW AND/OR FOREHEAD

Botulinum toxin type A and hyaluronic acid fillers are commonly used to correct rhytides in the brow and forehead area.[14,15] The neurotoxin botulinum toxin type A has been available for more than 20 years[16,17] and is approved for the temporary improvement of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity.[18] Additionally, botulinum toxin type A has been used to diminish the appearance of forehead lines and crow's feet as well as to elevate the eyebrows by changing the dynamic interrelationship of the muscles around the brow.[19] Although some authors recommend avoiding the injection of botulinum toxin type A below the orbital rim,[20] I have been using it at the level of superior orbital rim near the tail of the brow with great success. Also, as others have noted, botulinum toxin type A can be used in several other facial areas.[21-24] For example, in my own clinical practice, I have been applying it in platysmal neck bands to help reduce their activity, as well as for the correction of perioral rhytides. I also use it in patients with Bell palsy and facial paralysis to control synkinesis and symmetrize the facial appearance.

LOWER EYELIDS

Several hyaluronic acid derivatives are approved by the FDA for correction of moderate to severe facial wrinkles, such as nasolabial folds.[25-29] In addition, these agents have been used

to increase fullness in the brow area[30] and to correct tear trough deformity.[31-33] Cross-linking between carboxyl and N-acetyl groups enhances the viscosity of the naturally occurring hyaluronic acid, thereby increasing its stiffness and changing its water-retention properties.[30] Thus, after injection, some hyaluronic acid derivatives may continue to swell as they absorb water from surrounding tissues. However, these products are resorbed slowly over a period of 4 to 8 months. In describing their experience of administering 244 hyaluronic acid gel injections in 155 patients with periorbital hollows, Goldberg and Fiaschetti[31] noted that 89% of the patients were satisfied with the cosmetic improvement. However, hyaluronidase injections were necessary at follow-up visits to break down the hyaluronic acid which was thought to be the cause of contour irregularities in 15% of patients. Kane[32,33] reported the use of hyaluronic acid gel injections to treat tear trough deformity in a smaller patient population. Of 24 patients treated, only 2 were dissatisfied with the results and no patient required the use of hyaluronidase injections to correct irregularities. The injection technique described by Kane is designed to minimize the appearance of lumps or ridges when hyaluronic acid gel is used in this delicate skin area.[33] Following application of a topical anesthetic to the lower eyelids, the manufacturer-supplied needle is used to inject the dermatologic agent. The full length of the needle is inserted below the surface of the skin and minuscule threads of hyaluronic acid gel are injected below the orbicularis oculi muscle. In many individuals a minimal amount may also be injected in the plane between the dermis and the orbicularis oculi muscle in a crosshatched pattern. It is important to gradually decrease the amount of filler injected in the border areas in order to keep a smooth contour. Most patients require 0.3 to 0.5 mL of filler per eyelid, but more may be needed for deep depressions. Patients should be instructed to apply cold compresses to the area and keep their head elevated for 2 days following the procedure.[32,33] In my own practice, I generally inject hyaluronic acid products deep into the orbicularis oculi to avoid the Tyndall effect (bluish hue under the skin). I then use subcutaneous injections to even out fine irregularities.

CHEEK AND/OR LOWER FACE

Products used for volume restoration in this area of the face include injectable PLLA,[34,35] and calcium hydroxylapatite.[36,37] Hyaluronic acids and porcine collagen may also be used, depending on the goals of the patient. Injectable PLLA is a polymeric device that contains microparticles of PLLA, a biodegradable, biocompatible synthetic polymer from the -hydroxy acid family. Injectable PLLA is approved by the FDA for correction of the signs of facial fat loss (lipoatrophy) in patients with the human immunodeficiency virus (HIV).[38] Injectable PLLA is also approved for facial cosmetic use in Europe, Canada, and Australia.[34] Currently, an application for volume restoration and/or correction of facial wrinkles and folds such as nasolabial lines or folds is pending approval from the FDA.

In an open-label clinical study, patients with HIV-associated lipoatrophy experienced a 65% increase in skin thickness after undergoing a series of treatment sessions with injectable PLLA. This increase was maintained throughout a 12-month follow-up period.[39] The effects of injectable PLLA have a gradual onset and have been reported to last up to about 2 years.[34] Many of my patients have experienced an increase for up to 3 years. It is important to note that the safety and effectiveness of treatment with injectable PLLA in the periorbital area have not been established.[38] Therefore, only highly experienced practitioners should use injectable PLLA in this area.[40]

Calcium hydroxylapatite, consisting of 25 to 45 μm particles suspended in a gel,[41] is indicated for the correction of moderate to severe facial wrinkles, such as nasolabial folds, and the signs of facial fat loss (lipoatrophy) in people with HIV.[42] Because of the gel's viscosity, care must be used when injecting this device in facial sites.[43] Calcium hydroxylapatite is most commonly used to correct depressions in nasolabial folds, cheeks, deep glabellar creases, oral commissure, horizontal mental crease, and acne scars. It is a versatile product[44] that is also applied in the malar and submalar regions as well as the prejowl sulcus.[36] It should be injected into the immediate deep subdermal layer; more superficial placement increases the risk of visibility and nodule formation.[36]

In an open-label study,[44] calcium hydroxylapatite was associated with very good or excellent results in 90% of the 113 study participants; in this subgroup, 15 participants received injections into the cheeks, 86—into the nasolabial folds, and 26—into perioral lines. Adverse events were mild, resolved within 1 month, and were reported by a small number (7) of study participants.[44] In a separate study, 609 participants received a total of 1348 injections of calcium hydroxylapatite[45]; 112 participants completed satisfaction surveys at 12 to 14 months and 69% of them reported continuing satisfaction.[45] Postinjection lip nodules that

generally resolved with steroid injections or repeated massage occurred in 42 participants who had injections into the lip mucosa or radial lip lines.[45] Because it is liable to form lip nodules, calcium hydroxylapatite should not be used in the lip area. Furthermore, only a skilled practitioner should perform injections of calcium hydroxylapatite in the lower eyelid and nose. The use of injectables in the nose should only be done to correct contour irregularities in patients who do not desire to have rhinoplasty performed for the foreseeable future. In my practice, I utilize hyaluronic acids due to their reversibility and short duration only in a very small group of individuals who have minor contour irregularities.

ADDITIONAL NONSURGICAL PROCEDURES

Noninvasive, nonsurgical skin rejuvenation techniques and treatments, such as fractional laser resurfacing and medical grade topical skin-care agents, can be used in combination with the aesthetic procedures described above to enhance outcomes. The 1320-nm neodymium: yttrium-aluminum-garnet (Nd:YAG) laser (CoolTouch, New Star Lasers, Roseville, CA) emits infrared light that promotes dermal collagen synthesis. However, concern about possible distortion of the injectable collagen implants from the heat of laser treatments has limited their concomitant usage.[46] Goldman and colleagues determined that Nd:YAG laser treatment administered immediately after hyaluronic acid gel implantation did not result in a reduction of the clinical effect of either device; they also found that concomitant therapy was not associated with an increase in adverse event occurrence. Similarly, injection of botulinum toxin type A into the periorbital area either before or after erbium:YAG laser (Focus Medical, CT) resurfacing enhanced the improvement of periorbital rhytides as well as periorbital skin texture and pigmentation.[47] To further optimize the results of the selected procedure, skin-care regimens should be discussed with patients undergoing surgical or nonsurgical facial volume replacement procedures so that improvements can be maintained. Medical grade topical skin-care agents (“cosmeceuticals”) containing ingredients such as vitamin C, -hydroxy acids, retinoic acid derivatives, and skin growth factors may have beneficial effects on skin and slow the appearance of further signs of aging.[48]

CLINICAL RECOMMENDATIONS

In my own clinical practice, I have used multiple facial contour enhancement agents for patients who are not candidates for rhytidectomy and for individuals who do not wish to undergo surgical intervention. In my experience, certain agents and devices seem to perform most effectively when used in specific areas of the face. My agents of choice for specific procedures are botulinum toxin type A for periorbital rhytides, chemical brow-lift and platysmal banding; hyaluronic acid for lower eyelids and brow rejuvenation and for patients who desire immediate results; porcine collagen and calcium hydroxylapatite for cheek augmentation, nasolabial fold, and prejowl sulcus; and injectable PLLA for moderate to severe facial aging secondary to volume loss, especially in the mid face, cheek, and prejowl regions. Unlike other products, injectable PLLA offers a gradual onset of effect and long duration of action (for up to 2 years).[49] For skin rejuvenation, I prefer to use a combination of medical grade topical skin-care agents, as well as fractional laser resurfacing, to augment nonsurgical facelift procedures.

Figure 1

Table. Injectable Agents Used in Minimally Invasive Nonsurgical Face-Lift Procedures

Product	Manufacturer/Distributor	Indication
Botulinum Toxin Type A		
Botox Cosmetic[18]	Allergan Pharmaceuticals Ireland, a subsidiary of Allergan, Inc., Irvine, CA	For the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients ≤65 years
Hyaluronic Acid Derivatives		
Hylaform[26]	Genzyme Biosurgery, Ridgefield, NJ/Inamed Aesthetics, Santa Barbara, CA	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (eg, nasolabial folds)
Hylaform Plus[26]	Genzyme Biosurgery, Ridgefield, NJ/Inamed Aesthetics, Santa Barbara, CA	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (eg, nasolabial folds)
Juvéderm Ultra[27]	Corneal, Paris, France/Inamed Aesthetics, Santa Barbara, CA	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (eg, nasolabial folds)
Perlane[28]	Q-Med AB, Uppsala, Sweden/Medicis Aesthetics, Inc., Scottsdale, AZ	For implantation into the deep dermis to superficial subcutis for correction of moderate to severe facial wrinkles and folds (eg, nasolabial folds)
Restylane[29]	Q-Med AB, Uppsala, Sweden/Medicis Aesthetics, Inc., Scottsdale, AZ	For mid to deep dermal implantation for correction of moderate to severe facial wrinkles and folds (eg, nasolabial folds)
Calcium Hydroxylapatite		
Radiesse[42]	BioForm Medical Inc., Franksville, WI	For subdermal implantation for the correction of moderate to severe facial wrinkles and folds, (eg, nasolabial folds). For restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus
Porcine Collagen Gel		
Evolence[11]	ColBar LifeScience Ltd., Herzliya, Israel /OrthoNeutrogena, division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., Los Angeles, CA	For the correction of moderate to deep facial wrinkles and folds such as nasolabial folds
Poly-L-Lactic Acid		
Sculptra[38]	Dermik Laboratories, a business of sanofi-aventis U.S. LLC, Bridgewater, NJ	For restoration and/or correction of signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus

CONCLUSIONS

The number of patients desiring nonsurgical restoration of facial volume loss as a result of aging, trauma, or disease, is increasing. To address this demand, many plastic surgeons, facial plastic surgeons, and cosmetic dermatologists are creating their own combination regimens by using injectable devices based on their personal clinical experience with various agents. In my experience, botulinum toxin, hyaluronic acid, calcium hydroxylapatite, porcine collagen, and injectable PLLA have become the principal devices used for patients who are seeking nonsurgical restoration of facial contours.

ACKNOWLEDGMENTS

Editorial support was provided by the editorial staff at Embryon. Editorial support for this article was funded by Dermik Laboratories, a business of sanofi-aventis U.S. LLC. The opinions expressed in the current article are those of the author. The author gratefully acknowledges Patricia Bichler, PhD who assisted in the preparation of this article based on author-provided comments. The author received no honorarium or other form of financial support related to the development of this manuscript.

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