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Hyaluronic Acid Gel (Restylane) Filler for Facial Rhytids: Lessons Learned From American Society of Ophthalmic Plastic and Reconstructive Surgery Member Treatment of 286 Patients

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Purpose: To review injection techniques and patient satisfaction with injection of Restylane in various facial areas by American Society of Ophthalmic Plastic and Reconstructive Surgery members.

Methods: Data from 286 patients treated with Restylane in nine American Society of Ophthalmic Plastic and Reconstructive Surgery practices were abstracted to a spreadsheet for analysis.

Results: Nine practices performed Restylane injections for 8.8 months on average (range, 2 to 28 months). Average practice volume per patient was 1.2 ml (range, 0.7 to 2.1 ml). Nine of nine practices injected the nasolabial and melolabial folds, 9 of 9 practices injected the lips, and 6 of 9 injected the glabella. Only 2 of 9 practices injected other fillers concurrently. Botox was injected concurrently by 8 of 9 practices. On a scale of 1 to 10, physicians rated average patient discomfort during Restylane injection 4.6 with topical anesthesia and 2.1 with injectable lidocaine, with or without topical anesthesia. The end point for injection was determined by visual cues, volume of injection, extrusion of the product, and palpation. "Problematic" complications, including bruising, swelling, bumpiness, and redness each had an incidence of 5% or less. Patient satisfaction on a scale of 1 to 10 had an average rating of 8.1, compared with that of Botox injection (8.9), upper blepharoplasty (8.9), and collagen injection (6.6). The source of Restylane patients was estimated to be existing Botox patients (45%); existing non-Botox patients (18%); word of mouth (14%); and new patients for other services (13%).

Conclusions: Injection techniques, volume, end points, and anesthesia vary for different facial areas and between practices. Patients experience mild to moderate injection discomfort that is lessened with injectable lidocaine. Self-limited problems occur in about 5% of patients. Physician-determined patient satisfaction is perceived to be higher than that of collagen injection but slightly lower than that of botulinum toxin injection. The major source of Restylane patients was from existing practice patients, especially botulinum toxin patients.

Restylane (Medicis Aesthetics Inc., Scottsdale, AZ, U.S.A.) is a nonanimal, stabilized hyaluronic acid that is FDA approved for dermal implantation to correct facial wrinkles and folds. It is produced by bacterial fermentation and undergoes cross-linking to increase its tissue half-life. In contrast, Hylaform (Inamed Aesthetics, Irvine, CA, U.S.A.) is injectable hyaluronic acid derived from rooster combs. Because hyaluronic acid, unlike collagen, does not differ chemically from species to species,[1] it has a low risk of allergic reaction. Restylane is a viscous, transparent gel, composed of stabilized hyaluronic acid (20 mg/ml). The particle size is 250 millimicrons. Medicis Aesthetics Inc. also produces similar compounds with different particle sizes (Perlane, 1,000 millimicrons, and Restylane Fine Lines, 250 millimicrons), but Restylane is currently its only FDA-approved dermal filler.

Unlike injectable collagen fillers, Restylane does not contain a local anesthetic. Although it was initially sup-

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plied in 0.7-ml glass syringes, it is currently supplied in syringes containing approximately 1.0 ml or 0.4 ml of material. Restylane does not require refrigeration before injection, but each syringe is manufactured for single use, and the product does not have a preservative.

Restylane binds water and undergoes isovolemic degradation. As it is resorbed, the remaining Restylane molecules bind more water,[2] resulting in a longer-lasting fill than collagen injections. In fact, Restylane has been shown clinically to provide a more durable improvement in wrinkles than bovine collagen.[3] Furthermore, concurrent botulinum toxin injection has been demonstrated to improve and prolong the results of Restylane injection in the glabella.[4]

METHODS

The study was a multicenter retrospective review. Data from 286 Restylane patients treated in 9 American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS) practices were abstracted to a spreadsheet for analysis.

RESULTS

Respondents were ASOPRS members who had been in practice for an average of 13.1 years (range, 2 to 20 years). These practices were early adopters of Restylane and had performed Restylane injections for an average of 8.8 months (range, 2 to 30 months). One of the practices was not injecting any other dermal fillers. The other 8 all used collagen in some patients. Two of the 9 practices injected collagen in the same area concurrently with Restylane in some patients. The average volume injected per application was 0.8 ml or less. Other fillers in use in these 9 practices included collagen (7 practices), autologous fat and Radiance (2 practices each), and micronized Alloderm (one practice). Of note, none of the practices was injecting Hylaform at the time of the survey. Eight of 9 practices injected botulinum toxin concurrently. The average volume injected per patient was 1.2 ml (range, 0.7 to 2.1 ml). The average number of patients treated per practice and average volume injected for the most common applications are summarized in the Table. Typical results of treatment are demonstrated for the nasolabial folds (Fig. 1) and nasolabial folds and lips (Fig. 2). Other sites less frequently injected included depressed scar augmentation (3 practices) and submental furrow, cheeks, and alar retraction (one practice each). When respondents were asked about the maximum volume that could be safely injected in one setting, the average response was 2.9 ml (range, 1.4 to 5.0 ml).

When used, topical anesthetics were applied for an average of 36 minutes (range, 15 to 100 minutes). These included various formulations (e.g., topical lidocaine gel, benzocaine/lidocaine/tetracaine gel, and tetracaine gel). In all patients, the glabella was exclusively treated with topical anesthesia.

The nasolabial folds were pretreated exclusively with topical agents in all patients of four of the nine practices, and one practice used both injectable and topical anesthesia in all patients. Two practices used injectable anesthesia for all nasolabial folds and also used topical for 30%. Of the remaining two practices, one used supplemental local anesthesia and the other used half topical anesthesia and half local anesthesia.

For lip injection, 5 of the 9 practices used topical anesthesia

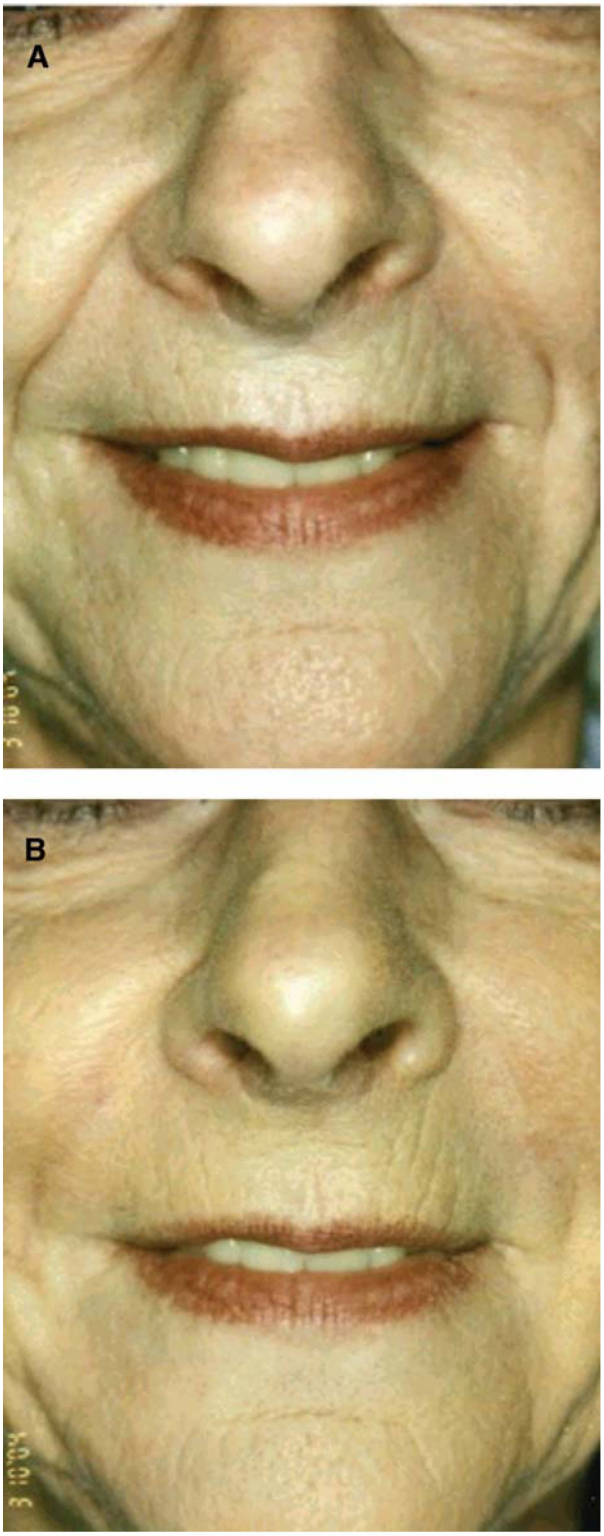

FIG. 1. Typical patient before **(A)** and after **(B)** Restylane injection to the nasolabial folds.

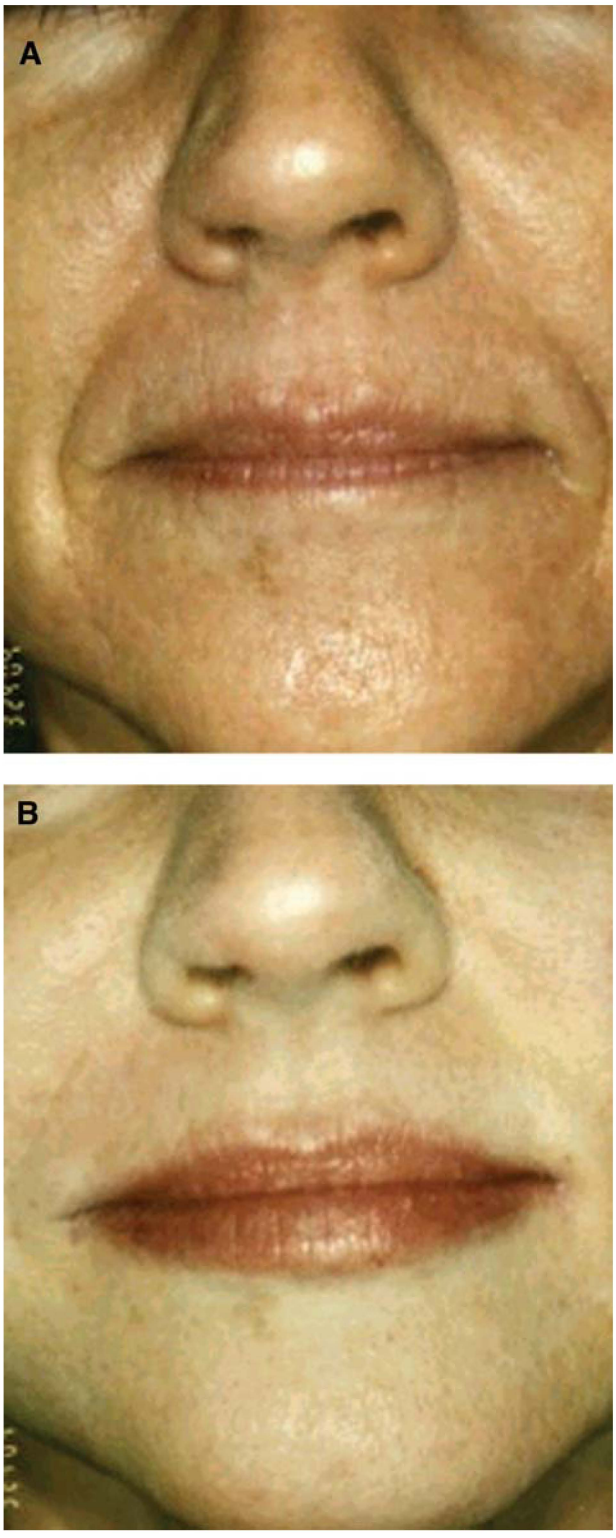

FIG. 2. Typical patient before **(A)** and after **(B)** Restylane injection to the nasolabial folds and lips.

in more than 75% of patients, and 5 of the 9 practices used injectable lidocaine in more than 75% of patients. Two practices used both topical and injectable anesthesia in all patients.

For melolabial fold (marionette lines) injection, one practice used both topical and injectable anesthesia, and the remaining practices used topical anesthesia exclusively.

Average volume per patient for most common sites

Application	Practices injecting	Patients/practice	Volume (ml)
Nasolabial folds	9	26	0.8
Melolabial folds	9	6	0.5
Vermillion border	9	22	0.5
Lip volume enhancement	8	18	0.6
Glabellar furrows	6	3	0.3

Protective wincing movements were reported in 20% of patients treated with topical anesthetic. The estimated patient discomfort scale averaged 4.6 of 10 for topical anesthesia and 2.1 of 10 for injectable lidocaine with or without topical anesthesia.

Commonly used injection techniques included serial puncture, linear threading, fanning, and cross-hatching. Most respondents (7 of 9) estimated the injection end point by visual cues. Other end points included volume of injection, extrusion of the product, and palpation.

Of the nine practices, one routinely administered prophylactic oral antiviral medication and six used antivirals for patients with a history of HSV. Two practices do not prescribe antivirals.

All complications occurred locally. "Problematic" complications included bruising (5%), swelling (4%), bumpiness (3%), asymmetry (3%), and redness (1%).

Physician respondents rated their perception of patient satisfaction after Restylane injection to be 8.1 on a 1 (low) to 10 (high) scale. The physician's perception of patient satisfaction after Restylane injection compared well with that of botulinum toxin injection (8.9), upper blepharoplasty (8.9), and collagen injection (6.6). Analysis of the source of Restylane patients revealed existing botulinum toxin patients to be the largest source. Other sources included existing non–botulinum toxin patients (18%), word of mouth (14%), and new patients for other services (13%).

DISCUSSION

An early analysis of 9 ASOPRS practices reveals that injection techniques, volume, end points, and anesthesia vary for different facial areas and between practices. However, patient satisfaction with Restylane injection is higher than that of collagen injection and comparable to that of botulinum toxin injection and upper blepharoplasty. Patients experience mild to moderate discomfort, which is lessened by injectable lidocaine.

At the time of the survey, the product was only available in 0.7-ml syringes, but it is now distributed in both 1.0-ml and 0.4-ml syringes. This change may affect the volumes that the participants now use for the various applications. As the number of applications for the product continues to grow, we find ourselves injecting higher total volumes as patients receive correction in multiple areas. Restylane may be injected at the same time as botulinum toxin, and concurrent injection of both products has been shown to increase the longevity of

Restylane.[4] During injection, patients may experience mild to moderate discomfort, which is lessened with injectable lidocaine for most sites. When injections are used for the lips or nasolabial folds, we recommend injecting lidocaine to balloon the mucosa of the gingival sulcus in the plane of the third tooth from the midline. This plane corresponds to the infraorbital nerve superiorly and the mental nerve inferiorly. Our preferred injectable anesthetic is lidocaine 2% with epinephrine 1:200,000 injected as 0.5 to 1.0 ml at each site. Self-limited complications occur in approximately 5% of patients.

In summary, we found Restylane to be a safe, predictable, and effective treatment for static wrinkles. We await the results of long-term experience with the inclusion of additional areas such as the eyebrows and tear trough.

REFERENCES

1. Larsen NE, Pollack CT, Reiner K, et al. Hylan gel biomaterial: dermal and immunologic compatibility. *J Biomed Mater Res* 1993; 27:1129–34.
2. Goa KL, Benfield P. Hyaluronic acid: a review of its pharmacology and use as a surgical aid in ophthalmology, and its therapeutic potential in joint disease and wound healing. *Drugs* 1994;47:536–6.
3. Narins RS, Brandt F, Leyden J, et al. A randomized, double-blind, multicenter comparison of the efficacy and tolerability of Restylane versus Zyplast for the correction of nasolabial folds. *Dermatol Surg* 2003;29:588–95.
4. Carruthers J, Carruthers A. A prospective, randomized, parallel group study analyzing the effect of BTX-A (Botox) and nonanimal sourced hyaluronic acid (NASHA, Restylane) in combination compared with NASHA (Restylane) alone in severe glabellar rhytides in adult female subjects: treatment of severe glabellar rhytides with a hyaluronic acid derivative compared with a hyaluronic acid derivative compared with the derivative and BTX-A. *Dermatol Surg* 2003;29:802–9.