Volumizing with a 20-mg/mL Smooth, Highly Cohesive, Viscous Hyaluronic Acid Filler and Its Role in Facial Rejuvenation Therapy

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BACKGROUND The new 20 mg/mL hyaluronic acid (HA) dermal filler is a smooth, highly cohesive, viscous formulation developed to restore volume in aesthetic facial rejuvenation.

OBJECTIVE Evaluate clinical experience with 20 mg/mL HA dermal filler to date and comment on its current and potential uses within the facial rejuvenation treatment paradigm.

METHODS AND MATERIALS In this paper, the authors review the unique physical and chemical properties of 20 mg/mL HA dermal filler as well as clinical experience with the product to date.

RESULTS Overall, the 20 mg/mL smooth, cohesive, viscous HA filler was especially effective in restoring volume in the malar region and chin. Volume loss resolved significantly in patients in clinical trials¹ and treatment effects were observed to be maintained from six to 18 months.² Physicians reported the agent was highly effective as well as easy to inject, sculpt and mold. The treatment was generally well tolerated and no instances of product migration from the injection site have been reported. Patient satisfaction was high, with the vast majority of trial participants acknowledging they would return for additional treatment and recommend the treatment to friends.¹,²

CONCLUSION Initial experience shows the 20 mg/mL smooth, cohesive, viscous HA filler to be a useful addition to the facial rejuvenation armamentarium when used both alone and in combination with BTX-A.

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Background

The past decade has seen an explosion of new products and techniques, such as botulinum toxin type A (BTX-A) and hyaluronic acid (HA) subdermal fillers, which has allowed clinicians to achieve increasingly precise, versatile, and aesthetically pleasing outcomes. Patient satisfaction and demand for treatment has increased exponentially as a result.¹–³

The traditional focus was on a two-dimensional plane, using BTX-A to immobilize muscles associated with hyperdynamic wrinkles and using fillers superficially to reduce wrinkles. There is now a greater appreciation of the need to address the three-dimensional effects of aging, particularly those caused by volume loss. Current approaches combine volumizing and contouring with movement control, using BTX in combination with HA fillers to achieve results that are longer lasting and more satisfying to patients.³

Volume restoration then, is critical to successful facial rejuvenation. It is used to replace or augment soft tissue specifically in the deflated malar and

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zygomatic regions, brow, and infraorbital hollows. Treatment in these areas is required because of volume loss in the malar fat pad and facial bone remodeling and shrinkage. The enlarging envelope of facial skin begins to sag because of the loss of support from the underlying fat and bone tissues.3–5

There are many benefits of using HA fillers in facial rejuvenation. Effects are visible immediately after treatment and include a glowing hydrated appearance of the skin over the injected regions. Patients can return to their normal activities on the same day. Adverse immune reactions to HA fillers are rare because HA has a uniform structure throughout all species, and the clinical products are produced from bacterial (not human or animal) sources in the laboratory.2

20-mg/mL Smooth, Cohesive, Viscous HA Filler

Two parameters—the linear viscosity (a function of elastic modulus or $G'$) and the cohesivity of the gel—determine the lift or volumizing capacity of an HA dermal filler. In terms of relative contribution to lift capacity, both parameters play a role of equal importance. The 20-mg/mL smooth, cohesive HA filler (Juvederm Voluma, Allergan Inc., Santa Barbara, CA) has a unique combination of high cohesivity and high viscosity, which gives it a greater lift capacity than most other HA fillers. As such, it is ideally suited for volumizing and contouring.1 Juvederm Voluma is approved for use in Canada and is under clinical trial investigation in the United States and other markets. The base HA material is derived from bacterial fermentation by Streptococcus equus.2 Although most HA fillers are derived from high-molecular-weight (HMW) HA ($\sim 1$ MDa), the 20-mg/mL smooth, highly cohesive, high-viscosity gel uses a mix of low-molecular-weight (LMW; <1 MDa) and HMW HA polymer chains as its raw material source. The addition of LMW HA, allows the use of less cross-linking agent, 1,4-butanediol diglycidyl ether to achieve a high linear viscosity ($G'$ is 330 Pa at 5 Hz) while maintaining a relatively high cohesivity. Through the coupling of high viscosity and high cohesivity, it is able to retain its structure without migration from deep injection sites. The use of LMW HA requires minimal amounts of uncross-linked (nonmodified HA chains and lightly cross-linked chains and fragments in soluble form) HA (a lubricant) within the end product, which has a positive effect on extrusion properties. In contrast, particle suspension HA fillers have higher viscosity levels, requiring more uncross-linked HA (Allergan, data on file), which may explain their greater tendency to migrate from the injection site.6 Those fillers are also firmer and less force is required to inject. Like all other HA fillers, the effects of the 20-mg/mL smooth, highly cohesive, viscous gel are fully reversible with hyaluronidase and therefore correctable. This is useful in case of product misplacement or over-volumizing and is a significant benefit over other fillers such as bovine collagen, poly-L-lactic acid, and polymethylmethacrylate.6,7

Overall, the 20-mg/mL smooth, highly cohesive, viscous HA filler was developed to have a high lift capacity for volumizing. Although it is a robust subdermal filler, it nonetheless has a smooth consistency and is easy to inject and mold. In the context of the spectrum of HA fillers (distinguished according to their varying degrees of viscosity and lift capacity), this product is well suited for correction of deeper wrinkles and folds as well as volumizing and contouring. Less viscous gels may be preferred for correcting relatively fine, superficial lines, in lip enhancement, or in thin-skinned areas such as the tear trough.6

Clinical Experience

The 20-mg/mL smooth, cohesive, viscous HA filler has been evaluated in a prospective study of 70 patients and in a retrospective analysis of records of 102 patients. Investigators and patients in both
evaluations concluded that Voluma was highly effective, easy to use, and well tolerated.

Allergan, Inc. funded the prospective trial, conducted by Klaus Hoffmann for the Juvéderm Voluma Study Investigators Group. In this open-label, nonrandomized study, 15 physicians (dermatologists, plastic surgeons, and aesthetic practitioners) evaluated the 20-mg/mL smooth, highly cohesive, viscous HA filler within its indicated use of restoring facial volume in 70 patients (Figure 1). The majority of these were women with a mean age of 50 and a somewhat greater than moderate loss of volume on the 5-point Facial Volume Loss Scale (1 = mild, 2 = intermediate between mild and moderate, 3 = moderate, 4 = intermediate between moderate and severe, 5 = severe).

Investigators injected the 20-mg/mL smooth, cohesive viscous HA filler with a needle or cannula according to their usual practices. Injection sites included the malar area (59%), nasolabial fold (21%), chin (9%), temporal region (7%), and other (5%). The volume of injection was determined according to patient self-assessment on the Facial Volume Loss Scale.

Physicians assessed the ease of injection, sculpting, and shaping with the product and recorded their willingness to recommend the product to colleagues after the trial.

Effectiveness was determined based on investigator-assessed changes from baseline on the Facial Volume Loss Scale and patient ratings on the Global Aesthetic Improvement Scale (five categories ranging from very much improved to worse).

Patients rated their satisfaction with the overall cosmetic effect, their likelihood of returning for additional treatment, and their willingness to recommend it to friends.

Most injections were performed under local anesthesia, and needles were used in the majority of treatments. The most common treatment area was the malar region, and the mean total injection volume per patient was 4.6 mL. Regardless of technique, treatment area, or specialty, 95.6% of physicians found the 20-mg/mL smooth, cohesive, viscous HA filler easy to inject, sculpt, and mold.

Statistically significant improvements in facial volume were noted; 70% of patients were rated as having a low degree of volume loss after treatment, a substantial change from pretreatment (Figure 2). The majority of patients experienced no adverse events; 24 experienced injection-site reactions lasting a mean duration of 5.5 days. Patient ratings reported a high likelihood of returning for treatment (92%) and recommending it to friends (98%), indicating a high degree of patient satisfaction (Figure 3).

The results of the prospective trial are consistent with those of the retrospective analysis of 102 cases performed by Hervé Raspaldo and published in 2008. In contrast to the Hoffmann study, some of the cases reported results from combination treatments using the 20-mg/mL smooth, cohesive, viscous HA filler with BTX-A. Long-term results were also recorded; investigators observed low volume loss scores after treatment that persisted for 6 to 18 months. One of the advantages of a successful product is that techniques of insertion may vary with the preferences of the injector. Many physicians
Figure 2. Volume loss ratings on the Ascher Scale.

Figure 3. Physician and patient ratings on the Global Aesthetic Improvement Scale.
prefer to use a needle and others a cannula, but the results appear equally successful.

Raspaldo concluded that the results of the case analysis indicate that the treatment “results in clear aesthetic improvements comprising a pleasing, attractive mid-face area that resulted in increased self-esteem and greater confidence in the majority of patients, according to both the investigator and patient assessment, for up to 18 months post-treatment.”

For volumizing injections in the midface, the typical cheek requires 0.5 to 2 mL of the 20-mg/mL smooth, cohesive, viscous HA filler. We like to use a 28-G needle, and the location of the needle is deep—immediately preperiosteal. We use the anterograde injection technique (also called the “push ahead” technique) so that the product creates the support within the tissues without the needle tip inadvertently lacerating a blood vessel and causing a bruise. We inject with the patients in the sitting position so that gravity drapes the facial skin equally, which allows us to achieve the best symmetry (Figure 4).

Subjects may require product insertion more laterally to enhance the zygomatic region and more medially to lift the medial malar area or in the inferior cheek. In addition, we volumize the chin and the melomental region, if required (Figure 5).

Although not yet formally evaluated in volumizing of the brow, the 20-mg/mL smooth, highly cohesive, viscous HA filler is potentially an effective option in this application.

Aging eyes have traditionally been treated using surgical removal of excess skin and fat and sometimes elevation of the brow, but this method parallels (rather than counteracting) the effects of aging on the eye area.

The younger eye tends to be horizontal, long, and full without much upper lid showing. The more tissue that is removed or atrophies from the upper lid, the more the bony orbit becomes visible and the more rounded and hollow the upper lid appears. This extends the vertical height of the eye, shortening its horizontal appearance. In some cases, an A-frame deformity can develop—when superomedial hollowing occurs giving the patient an anxious appearance.

Recently, clinicians have found that improvements in the appearance of the eye area can be achieved by adding volume to the brow. An expanded brow reflects more light, eliminating shadows that
can cause a hollowed appearance. Even a small correction can make a large difference in the emotional projection and general balance of the facial features.

The best results can be achieved with HA filler. Although it has not been systematically studied in this indication, aesthetically pleasing and durable (>2 years) results have been achieved in our practice. Volume injections are highly technique dependent, and caution should be exercised not to over-correct, for fear of creating an abnormal or primitive look.

Discussion

Within the spectrum of HA dermal fillers, the role of the 20-mg/mL smooth, cohesive, viscous gel is clear. The higher viscosity of this product coupled with high cohesivity makes it an ideal agent for restoring volume in facial rejuvenation treatment. As we have seen, clinical experience has shown the product to be effective at restoring volume in the cheek and cheekbone areas and chin. As clinical experience with this product increases, additional volumizing applications, such as in the brow, may be included in its uses. Given its propensity to maintain its shape after injection, the 20-mg/mL smooth, cohesive, viscous HA filler may also be considered for the treatment of deeper lines and folds and has been demonstrated effective in diminishing the appearance of the nasolabial fold.

Physicians who have participated in trials of this product have remarked that it is easy to inject, sculpt, and mold. There were no reports of product migration, which contrasts with clinical experience with particle suspension gels. This may be a consequence of the homogenization process used during the manufacturing that produces the 20-mg/mL smooth, cohesive, viscous HA filler and other more fluid members of the same HA dermal filler family. The homogenization process tends to result in a smoother-consistency filler than granular dermal fillers, which are sized in a sieving process and have a granular consistency. The smooth flow properties of these gels allow gentle, gradual injection of product to the treatment area and facilitate precision of product placement.

Conclusions

Initial experience indicates the 20-mg/mL smooth, highly cohesive, viscous HA filler is
a useful new addition to the facial rejuvenation treatment armamentarium. It is formulated to provide a robust lift capacity, which makes it ideal for restoration of facial volume loss. Its ability to maintain its shape after deep injection also makes it suitable for deep wrinkles and folds. The product has been tried alone and in combination with BTX-A and other HA gel fillers, and treatment effects have been observed to persist for 6 to 18 months.

Clinical experience with the product at the time of writing has been extremely favorable. Physicians have reported the agent to be highly effective and easy to inject, sculpt, and mold. The treatment was generally well tolerated, and no instances of product migration from the injection site have been reported. Patient satisfaction was high, with the majority of trial participants indicating that they would return for additional treatment and recommend the treatment to friends.

These conclusions are based on clinical experience to date to provide clinicians with information about this new 20-mg/mL smooth, cohesive, viscous HA gel. Additional empirical evidence from further clinical trials is needed to validate these observations.

Acknowledgments This paper discusses published and/or investigational uses of agents that are not indicated by Health Canada. Allergan, Inc. does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

References

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