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Clinical application of a new hyaluronic acid filler based on its rheological properties and the anatomical site of injection

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Abstract

Background: Hyaluronic acid (HA) filler is the most commonly used filler for soft tissue augmentation. There are numerous commercially available HA fillers in the cosmetic market, and there are guidelines for each filler as determined by the manufacturing company. The successful use of injectable fillers requires an understanding of each option available so that the most appropriate form of hyaluronic acid may be selected for patients. The purpose of this study was to determine whether newly developed HA fillers are appropriate for forehead augmentation considering their rheological properties and the anatomical site of injection.

Methods: The rheological properties of new HA fillers were assessed e.t.p.q. S100, S300, S500 (Zetema®). Comparing the rheological properties, the authors chose e.t.p.q. S300® for forehead augmentation. The filler was injected into the foreheads of 40 consecutive patients for esthetic purposes.

Results: e.t.p.q. S300® was determined to be an appropriate filler for the forehead. The injection procedure employed was considered to be easy and safe when applied to the preperiosteal layer using a cannula. None of the patients had complications such as vascular compromise, infections, granulomas, or migration.

Conclusions: Understanding the physical properties of new fillers is necessary. As the preperiosteal layer of the forehead is an appropriate layer for the filler injection, physicians should consider injecting fillers with enough strength to withstand the shearing forces.

Keywords: Hyaluronic acid, Filler, Rheology

Background

The relationship between the forehead and nose is one of the most important factors for determining good external facial contours. In particular, a flat or depressed forehead makes it difficult to create a favorable side profile.

It is crucial to understand the anatomy to augment the forehead using hyaluronic acid (HA) as a soft tissue filler (Rohrich and Pessa 2007; Cotofana et al. 2017). An injection in the subcutaneous layer can lead to contour

irregularities and a relative risk of vessel damage. The HA filler injection is recommended to be injected into the preperiosteal layer behind the frontal muscle. When injecting a soft tissue filler behind the frontal muscle layer, the filler must have sufficient lift to withstand the compressive pressure of the frontal muscle. Therefore, it is important to choose the appropriate filler to withstand compressive and shear forces.

Nevertheless, there is a shortage of objective data for all available fillers, and physicians generally choose fillers according to the doctor's experience or company guidelines. When new filler products are introduced for clinical use, it is important to determine the layer into which they can be injected and to consider whether the

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physical and rheological properties of the product are appropriate for the target site anatomy.

We have studied the rheological properties of new hyaluronic acid fillers. Based on rheological studies, we selected HA fillers to improve the esthetics of the forehead and confirm if they have good lifting capacity.

Methods

Patient and methods

A total of 40 consecutive patients who underwent HA filler injection for esthetic reasons between March 2018 and June of 2018 at a private clinic were identified through a retrospective review of medical charts and evaluation of clinical photographs and were included in the study. All patients had opted for the injection for esthetic purposes. A single practitioner performed all procedures. The need for informed consent was waived by the institutional review board of Cheil General Hospital because of the retrospective nature of the study.

MCR 301 rheometer (Anton Paar Company, Graz, Austria) was used for the tests. The properties were measured from 1 to 0.02 Hz. The diameter of the plate of the rheometer was 2.45 cm, and the temperature was measured at 25 °C. A total of five fillers, Restylane®, Juvederm Volbella®, and e.t.p.q. S100®, S300®, and S500® were evaluated and compared for rheological tests (Table 1). Rheological test results are known to vary based on the different conditions of the materials. However, we evaluated each material in the same conditions and subsequently chose e.t.p.q. S300® for the procedures. e.t.p.q. S300® is a known monophasic filler (depends on its manufacturing process) and has a relatively high cohesiveness. The rheological test results of e.t.p.q. S300® are shown below (Fig. 1). The results were assessed subjectively by the patients by using a questionnaire, in which the patients were asked to rate their degree of satisfaction in terms of result and treatment convenience based on a 4-point scale (0, worse; 1, little satisfaction or not satisfied; 2, satisfied; and 3, very satisfied). The questionnaire was given to the patients at the end of the treatment, and again 15 days later.

Procedure

Patients underwent forehead augmentation with e.t.p.q. S300® (Zetema®). The amount of filler injection varied

from 2 to 5 cc. The entry points were made above the eyebrow and laterally from the mid-pupillary line. Local anesthetics were injected in the supratrochlear and supraorbital nerve regions. The filler was injected with a 22-G cannula. The cannula was inserted through an entry point and was placed deep behind the frontalis muscle, and the end of the cannula was located at the region where the filler was supposed to be injected. The procedure was performed gently, especially around the medial portion. Preoperative and postoperative photographs were compared (Fig. 2). Patient satisfaction was determined through a questionnaire.

Results

During the study period, a total of 40 patients (all women, ages 31.3 years [21–55]) underwent forehead augmentation, and each of them received 2–5 cc of the HA filler. All patients were injected into the suprapariosteal layer. All patients were pleased with the esthetic results. Of the 20 patients, 18 rated the results with 3 points, and the remaining 2 patients scored 2 immediately after injection. The satisfaction assessment performed 1 month after the procedure revealed that 19 patients were very satisfied and 1 was satisfied. The new e.t.p.q. S300® HA filler was determined to be an appropriate filler for the forehead. None of the patients experienced bleeding, hematomas, bruising, or vascular compromise. In addition, no patients had delayed filler migration, granulomas, or delayed swelling. The average follow-up time was 3 months (range from 1 to 12 months).

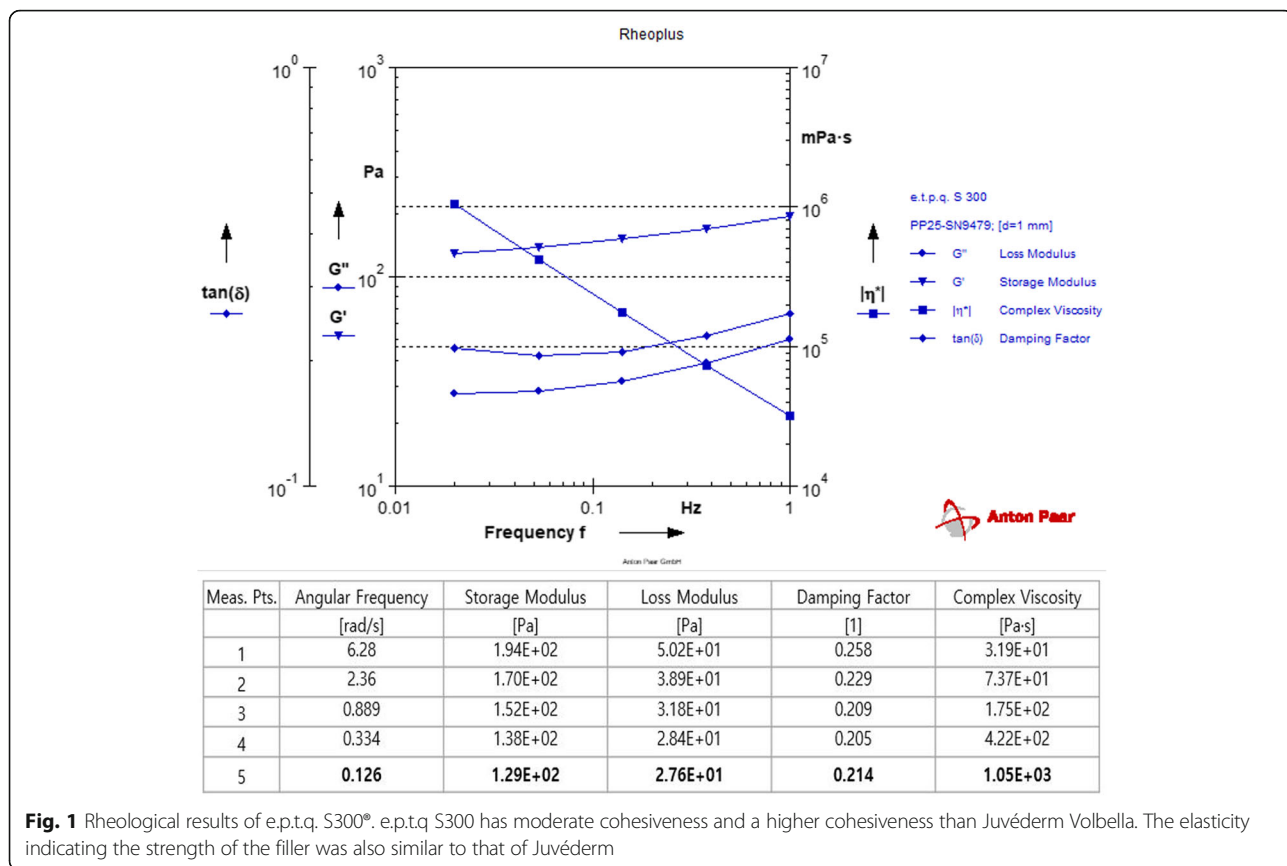
Discussion

The purpose of this study was to determine if the newly developed HA filler was suitable for forehead augmentation considering the anatomy of the forehead and the properties of the filler.

HA fillers are the most commonly used soft tissue filler. Since HA has a dermal component, it was initially used as a dermal filler; however, it has gradually been used for augmentation purposes. There are several limitations of dermal fillers with respect to the augmentation purposes. The filler should be injected into the deeper layer of the dermis for augmentation. When injected into the subcutaneous layer, the risk of vascular

Table 1 Rheological property of hyaluronic acid fillers

| Product | G' (Pa) | G'' (Pa) | Complex viscosity (cP) | Cohesiveness (M) | Tan δ | Complex modulus | Elasticity (%) |
|-------------------|---------|----------|------------------------|------------------|--------------|-----------------|----------------|
| Restylane | 349 | 145 | 3,011,188 | 0.3509 | 0.4180 | 378 | 71 |
| Juvederm Volbella | 99 | 21 | 814,593 | 0.3046 | 0.2189 | 101 | 83 |
| e.t.p.q. S100 | 37 | 15 | 323,859 | 0.4184 | 0.4269 | 40 | 71 |
| e.t.p.q. S300 | 128 | 27 | 1,048,864 | 0.6102 | 0.2137 | 131 | 83 |
| e.t.p.q. S500 | 224 | 57 | 1,847,607 | 0.8776 | 0.2551 | 231 | 80 |



complications, such as vascular compression or occluding blood vessels, increases. Therefore, many doctors recommend injecting into a deeper layer than the subdermal layer to prevent such complications.

In the forehead, the filler can be injected in the subcutaneous layer in front of the frontalis muscle and in the preperiosteal layer in the back of the muscle. In the case of the subcutaneous layer, it is easier to make the desired shape in front of the muscle, but because of the vascular distribution, it is injected in the preperiosteal layer, which is mainly behind the muscle, thereby

reducing the risk of side effects. A recent topographical study regarding forehead filler injections also suggested that the supratrochlear and supraorbital arteries, which are critical anatomical structures, should be avoided during the injection procedure (Cong et al. 2017). Some doctors insist on injecting filler into the postperiosteal layer for forehead augmentation, but it is difficult to ensure the space for the filler injection between the periosteum and skull. It is equally difficult to inject the filler into the preperiosteal layer, but the preperiosteal layer is relatively safe and is clinically the most commonly used



layer, as shown in the previous anatomical studies (van Loghem et al. 2017).

When injecting for augmentation purposes, the physical properties of the filler as well as the layer to be injected in should also be considered. Fillers used for lifting purposes should have enough lift capacity and longevity. Additionally, they should not migrate a few months after the injection. To understand the physical properties of fillers, physicians should consider the concentrations, injection forces, particle sizes, difference in the manufacturing processes, and rheological properties. Rheological properties are known as objective parameters for soft tissue fillers. Among the rheological properties, G' is known for storage modulus and cohesiveness, which are important parameters for soft tissue filler properties (Pierre et al. 2015). Cohesiveness can be defined as a resistance to compression/stretching forces in a vertical plane once the product is implanted (Hee et al. 2015). When the physical properties of a filler are too soft, a filler can spread relatively, making it difficult to shape the target area. On the other hand, if a filler is too rigid, the projection can be represented well, but when applied to a relatively broad area such as the forehead, it becomes difficult to attain the desired shape. All the fillers could be used in the forehead, but the appropriate filler was determined on the basis of the results of the rheological study in this study. In the rheological study, the results of e.t.p.q. S300 were not too soft and not too rigid either, and the volume was maintained well when the filler was injected. Therefore, the rheological profile of S300 was deemed appropriate.

In addition, the characteristics of the site should be considered when injecting the filler for augmentation purposes. This includes the anatomic layer to be injected as described above, the difference in skin thickness along the face, and finally the desired shape of augmentation (Ha et al. 2005). For example, for chin augmentation, the post-implant chin should have a relatively limited area and should have its center raised. This implies that the filler must be injected into the deep layers, and a cohesive and rigid filler should be selected. However, augmentation in the forehead covers a relatively large area. A filler that spreads more widely is suitable for this purpose in contrast to a filler that remains limited to a specific area. We suggest that for patients considering a chin augmentation, a very rigid e.t.p.q. S500 would be a good candidate. For the forehead, we suggest the e.t.p.q. S300 as the purpose is to augment a relatively broader area. Based on the test results, the e.t.p.q. S300 exhibited sufficient cohesiveness and elastic moduli in our study. Considering only the G' elastic modulus, S500 may be appropriate, but the forehead is different from the nose and chin, so projection is important, as is cohesiveness because it needs to be injected in a broader area. S300

has moderate cohesiveness compared with Restylane, one of the most commonly used HA fillers for forehead augmentation, and has a higher cohesiveness than Juvéderm Volbella.

When injected in the forehead, it has moderate cohesiveness, which makes the molding easier and migration less likely. The elasticity indicating the strength of the filler was also similar to that of Juvéderm. Therefore, it is considered to be a comparatively suitable filler for forehead augmentation.

Based on the rheological test, the e.t.p.q. S100 is also a good candidate for easy injection. However, since the HA modification value is high for e.t.p.q. S300, it can be maintained longer.

Conclusions

In cases of forehead augmentation, the preperiosteal layer is considered the most suitable layer for injection; thus, a sufficiently strong filler must be considered to withstand the shearing force.

Availability of data and materials

The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

Authors' contributions

WL contributed to the conceptualization, methodology, investigation, preparation, and writing of the original draft. JHY and ISK contributed to the conceptualization, writing, review, and editing of the draft. WO and KWK contributed to the formal analysis, preparation, and writing of the original draft. EJY contributed to the review and editing of the draft. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The need for informed consent was waived by the institutional review board of Cheil General Hospital because of the retrospective nature of the study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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