

Hybrid Nasal Filler: Combining Agarose Gel and Hyaluronic Acid for Nonsurgical Rhinoplasty

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Introduction: Given its structural properties, it would be a mistake to assume that a single type of filler fits perfectly to each anatomical region of the nose in nonsurgical rhinoplasty procedures. Therefore, we aimed to develop a hybrid treatment model by applying two different structural types of fillers. Hyaluronic acid (HA), a hydrophilic material, and agarose gel (AG), a nonhydrophilic and high G-prime material, were used in the study according to their advantages and disadvantages.

Methods: Patients who presented to the office desiring filler treatment for nonsurgical correction of the nose in a 2-year period were enrolled in the study. HA was used intradermally 0.1 ml per each point in the tip defining points and supratip. Injections of 0.4–0.7 and 0.4–0.6 ml AG were used supraperiosteally in the radix and nasal spine, respectively. Clinical improvement was evaluated two weeks later using the Global Aesthetic Improvement Scale from 1 to 5 (1: exceptional improvement; 5: worsened patient). Patient satisfaction was evaluated on a scale from 0 to 10 (0: not satisfied; 10: very satisfied).

Results: A total of 32 patients (mean age: 27 years) were enrolled in the study. Mean score of patient satisfaction was 9.09 of 10 after injection and 9 of 10 after 2 weeks. Clinical evaluation scores after injection were 1.72 of 5 and 1.69 of 5 on the Global Aesthetic Improvement Scale. No major complication was observed.

Conclusion: The HA and AG filler hybrid concept applied in different anatomical locations represents a safe and convenient option for nonsurgical rhinoplasty procedures. (*Plast Reconstr Surg Glob Open* 2022;10:e4236; doi: 10.1097/GOX.0000000000004236; Published online 6 April 2022.)

INTRODUCTION

Rhinoplasty is among the most commonly performed aesthetic procedures by plastic surgeons. Nonsurgical rhinoplasty is a procedure in which injectable fillers are applied to augment certain areas and temporarily change the shape of the nose to achieve improved appearance without a surgery in selected patients.¹ Although surgical rhinoplasty is the main procedure for reshaping the nose, nonsurgical rhinoplasty has recently become the first option for many patients and physicians.² This may be due

to the minimal downtime, less invasive nature, and low cost of these procedures compared to surgical cosmetic procedures.

Fillers are the most common nonsurgical method for volume correction.³ Dermal filler applications in the nose are mainly performed in two indications: (1) total dorsal augmentation (mostly in Asians or in those who have undergone an excessive reduction procedure to their nasal dorsum) and (2) injections to certain areas for nonsurgical aesthetic corrections and camouflage or to cover defects such as postoperative irregularities or deviations.^{4–6}

To obtain aesthetic results by injection into certain areas, injections are generally applied to four regions: (1) radix; (2) supratip; (3) tip; and (4) nasal spine. Radix and supratip injections are mostly made for hump camouflage; the rest are for tip rotation and projection.^{4–6}

Injectable fillers can be classified according to their various characteristics. Depending on the duration of the substance in the tissue, they can be classified as temporary, semipermanent, or permanent. Fillers also can be

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classified according to the product composition. The most common types are hyaluronic acid (HA), collagen, calcium hydroxylapatite, poly-L-lactic acid, polymethylmethacrylate, and agarose gel (AG).⁴⁻⁷

Even though there are some serious side effects and complications such as inflammation, granuloma formation, and tissue necrosis in the literature, most of the commonly used fillers have a good safety profile. It is important to choose the ideal filler considering the product properties. The ideal filler should be safe, biodegradable, long lasting, and easy to inject. It should also have minimal swelling and intratissue migration along with minimal or no allergic reaction.^{4,7,8}

The dorsal nasal arterial branches are located next to the the deep fatty layer and fibromuscular at the lower part of the dorsum. On the other hand, the dorsal nasal artery runs at the level of the superficial fatty layer of the procerus muscle just above the fibromuscular layer at the upper part of the dorsum (bony nose).⁹ Based on this vascular anatomical structure, suprapariosteal (subSMAS) injection planes in radix and nasal spine are the safest injection planes since there are vascular structures close to the skin in these locations.

In the tip and supratip areas, since vascular structures deepen, intradermal applications are relatively safe. Even if there is a subdermal plexus in the tip area, the main artery and veins are located on the surface of the nasal muscle structures and musculoaponeurotic structure.⁹

In current practice, HA fillers are the most commonly used fillers for nonsurgical rhinoplasty cases.¹⁰ HA has water retaining and swelling effects due to its hydrophilic nature, which is used in certain indications and good results can be obtained in this regard.¹¹⁻¹⁴ However, based on our experience, we can clearly state that these features negatively affect the predictability of the results that will occur during the application in today's facial suprapariosteal applications, for instance, in the radix and nasal spine.

Additionally, it has also been reported that filler migration can be seen in both early and late periods following facial deep soft tissue and/or suprapariosteal applications of HA. This situation may present undesired circumstances in terms of aesthetic and functional outcomes.¹⁵⁻¹⁸

Agarose is a material known for its different rheological properties.¹⁹ Its hydrocolloid and nonhydrophilic nature allow for accurate injections. It does not cause mid-term or long-term edema in the surrounding tissues.^{20,21} The nonhydrophilic, nonswelling, and minimal migrating nature of agarose represents a great advantage when it comes together with its high G-prime to give more definitive and better results by reshaping with minimal risks.²²

In our study, we aimed to develop a hybrid treatment model by applying two different structural types of dermal fillers given their advantages and disadvantages. To achieve this, we intradermally used fillers containing HA, a hydrophilic material, in cases where definition and augmentation were required for the nasal tip and supratip, respectively. Also, in cases where augmentation was required for the radix and elevation was required for the nasal tip, we suprapariosteally used fillers containing AG,

Takeaways

Question: Is it sufficient to apply the same type of filler to each area of the nose for optimal results?

Findings: Clinical evaluation results after injections showed exceptional or great improvement in GAIS. As for patient satisfaction results, 90.6% of the patients scored 8 or above (very satisfied) with respect to patient satisfaction results.

Meaning: We used different structural materials to anatomically different regions of the nose. AG and HA fillers can be used successfully with a hybrid combination and this concept represents a safe and convenient option for nonsurgical rhinoplasty procedures.

a nonhydrophilic material, so that it does not cause an undesired expansion by swelling, which may disrupt the aesthetics of the nasal root or narrow the airway by widening of the columella (Fig. 1).

MATERIALS AND METHODS

This study was approved by the university's clinical research ethics committee. (Approval codes: BSM43YL963, E.21698). Patients who presented to the office desiring filler treatment for nonsurgical correction of nose in the 2-years period were enrolled in the author's study. Patients unsatisfied with the appearance of their nose, specifically desiring correction for their dorsal hump, and requesting elevation-projection of their nasal tip were included in the study. Inclusion criteria consisted of patients who had not had any previous filler injections, threads, or related surgeries. Exclusion criteria consisted of patients who had conditions that could affect the outcome such as history of diseases affecting the immune system, active dermatological disorders (herpes, acne, and rosacea) or unhealed skin lesions, or pregnancy. All patients signed informed consent for the procedure and their photographs to be used in this study. The principles outlined in the Declaration of Helsinki (and later revisions) have been followed and conducted in compliance with good clinical practice.

Each procedure was performed in the office by the senior author, and the treatment time was approximately 20 minutes. The nasal area was cleansed with the antiseptic solution octenidine dihydrochloride. Two percent of lidocaine (0.2ml) was injected to nasal spine for local anesthesia and no anesthetic was used for other areas except in filler formulations such as HA containing lidocaine or that were mixed AG with 0.2 ml of 2% lidocaine.

After careful disinfection of the nose, the CE-certificated AG filler containing 3.5% agarose (Algeness Advanced Aesthetic Technologies, Brookline, Mass.) in a sterile syringe was mixed with 0.2 ml of 2% lidocaine in another syringe attached to the first syringe. The product was transferred from one to the other at least 20 times to obtain a favorable consistency.

Following that, AG was applied to the radix and nasal spine by perpendicular suprapariosteal injection. During

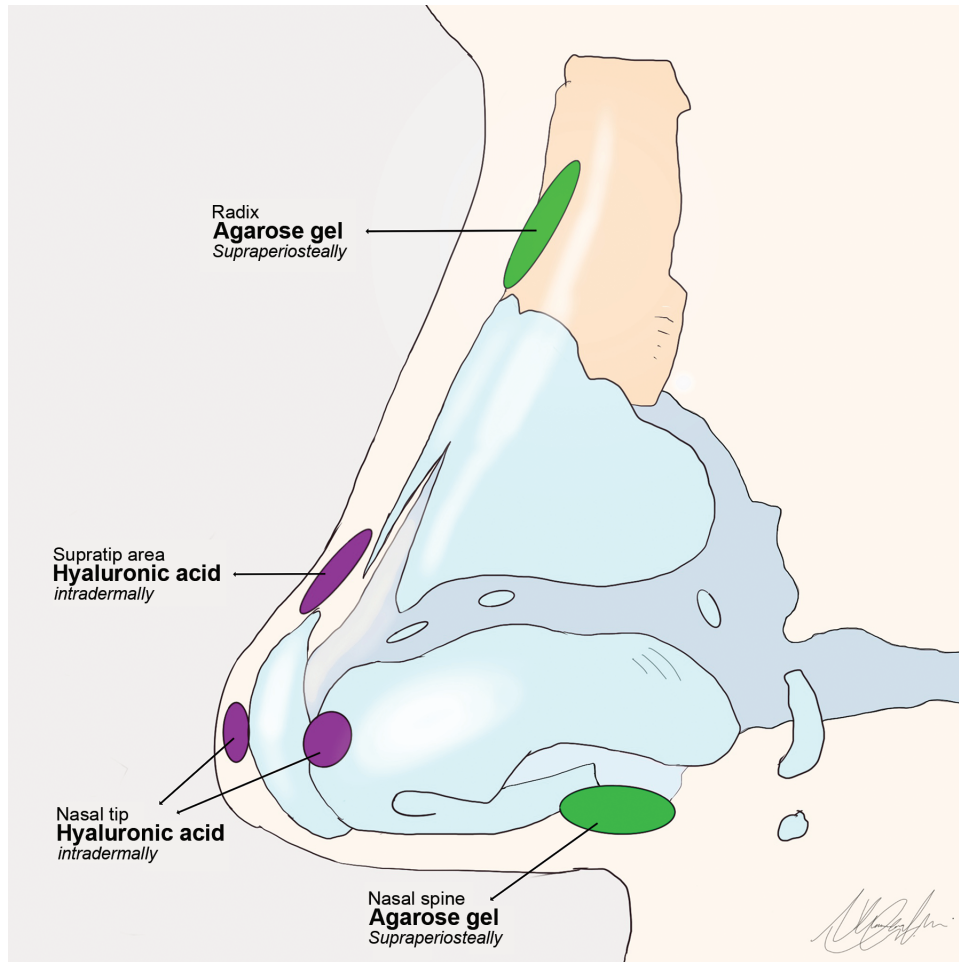


Fig. 1. Authors' four-point technique demonstrates hybrid treatment model by applying two different structural types of dermal fillers to anatomically different areas. An illustration shows important injection areas and injection planes that should be followed according to the filling material used.

the needle insertion, the skin of the nasal dorsum was gently lifted and compressed by nondominant fingers to minimize the embolization risk and migration. Columella was slightly elevated with the thumb and the second finger. Injections administered were approximately 0.4–0.6 ml for nasal spine and 0.4–0.7 ml AG for radix in small boluses per each location following the manufacturer's instructions. A 27-gauge and a 13-mm needle provided by the manufacturer were used for the injection. Aspiration for 5 seconds before the procedure is suggested in each application to avoid intravascular injection. Following the procedure, molding and positioning of AG was done by gentle massage and skin was taped with a sterile strip for a day. It was administered in clinical settings in accordance with the standard operating procedures.

After radix and nasal spine injections, under sterile conditions, the CE-certificated HA filler containing 20 mg HA with lidocaine (Yvoire Classic plus, LG Chem, Korea) was used for the tip defining points and supratip area intradermally, if necessary. Injections administered were approximately 0.1 ml per each point. A 32-gauge and a

4-mm needle were used for the filler injection. (See Video [online], which displays hybrid combination of HA and AG for nonsurgical correction of nose).

Patient satisfaction was evaluated on a scale from 0 to 10 using a survey and clinical improvement was evaluated using the Global Aesthetic Improvement Scale (GAIS) by two independent plastic surgeons immediately after the injection and at 2 weeks follow-up. Evaluators assessed the clinical images of patients before and after the injection.

The patients were evaluated two weeks after the injection to see if there were any complications or misplacement or revisional "touch-up" needed. Follow-up visits were on the first and sixth months after the injections.

Statistical Analysis

A descriptive analysis was performed. Categorical data were presented as numbers and percentages, and numerical data were presented with mean, median, and minimum-maximum values. Statistical analyses were performed using SPSS version 21.0 for Windows (SPSS Inc., Chicago, Ill.).

RESULTS

A total of 32 patients (mean age 27 years; range 19–44 years) who met the inclusion criteria were included in the author’s study. All of the participants were Caucasians. Sociodemographic characteristics of the patients are summarized (Table 1).

All of the patients were successfully treated. Clinical evaluation scores after injection were 1.72 of 5 and 1.69 of 5 on GAIS with 93.75% of the patients (30/32 patients) scoring 1 or 2 (exceptional or great improvement). Mean score of patient satisfaction was 9.09 of 10 after injection and 9 of 10 after 2 weeks with 90.6% of the patients (29/32 patients) scoring 8 or above (very satisfied). Study results can be seen (Table 2).

Preprocedure and 6 months postprocedure results can be seen after 3.5% Algeness injection (Figs. 2 and 3). Follow-up images showing the remaining clinical effect can be seen 10 months after 3.5% Algeness injection (Fig. 4).

At the end of the procedures, all patients had minor erythema and swelling at the injection site that resolved spontaneously within 24 hours. In only one patient, erythema in the tip area was observed for up to a week before disappearing.

Long-term follow-ups of patients were uneventful in terms of adverse events. No major complication was observed.

DISCUSSION

Nonsurgical rhinoplasty is an appealing procedure for many patients who are not ready for surgery or a long recovery period. Since the nose is located in the center of the face and contains anatomically high-risk areas, especially the nasal tip and glabella, it is important that

procedures are performed by experienced practitioners and that safe material is used.⁸

There are numerous fillers with different characteristics currently on the market. However, we believe that AG is a viable option with significant advantages in certain regions and indications besides HA or other alternatives.

The reason we prefer AG for the radix and the nasal spine is because it is hydrocolloid which allows precise injections with immediately visible results, and it has very little migration due to its non-reticular molecular structure.^{20–22} AG is nontoxic and free of crosslinking agents and chemicals. It does not contain any reticulating/crosslinking agents such as BDDE or any other chemical agent.²³ It is a completely biodegradable product and it is removed from the injection site by a process of macrophage phagocytosis and intracellular metabolization in the pentose cycle. This very special ability is what gives AG its safety.¹⁹ It is also necessary to be noted that most HA products, particularly the longer-lasting types, consist of highly reticulated HA. The long-term toxicity of these substances is not yet clearly understood.²³

AG does not have a swelling effect because of its non-hydrophilic nature and high G-prime.²² It does not cause an undesired expansion that may disrupt the aesthetics of the nasal root or narrow the airway by widening the columella; hence, it is possible to give better contour and definition. The clinical result can be positively affected from its slow resorption feature.²¹ Intradermal and big bolus injection of AG is not suggested to prevent palpability and lump formation. Although the linear retrograde injection is the preferred injection technique, serial small bolus injection on supraperiosteum has been found to yield good results. The risk of palpability can be reduced by gentle remodeling massage after the injection. It is suggested to apply more than it usually is in cases where HA is used.^{7,8} However, the HA filler can be applied intradermally to the tip and supratip area which can expand the skin and gives an opportunity to provide safer and better correction by using a smaller amount of filler due to its hydrophilic nature, especially in the tip defining points instead of the widening effect at the nasal tip by interdermal or subdermal injections.^{24,25}

Given the persistency of the fillers, it was stated in a study with a 2-year follow-up that 3.5% AG fillers could last up to 18 months. This result is comparable to similar HA products currently on the market.⁷

Sensitivity, erythema, swelling, and tenderness can be seen around the injection site after AG injections. These findings are temporary and are expected to disappear within a few hours or a few days. Immediately after injection, some skin redness may occur and is normal. Temporary erythema in the nasal tip area can be seen after intradermal HA injections, which can last up to a few weeks.

One of the main concerns with fillers is the risk of intravascular injection of the filler.²⁶ Expected findings of potential vessel occlusions are blanching, prolonged erythema, ecchymosis, intense pain, ischemia, and tissue necrosis.²⁷ For HA, we know that hyaluronidase

Table 1. Sociodemographic Characteristics of the Patients

Demographic Data	Treatment Group (%)
No. patients (n)	32
Gender	
Male	5 (16)
Female	27 (84)
Age, y	Mean age: 27
	Range: 19–44
19–24	15 (47)
25–44	17 (53)
Marital status	
Single	25 (78)
Married	5 (16)
Divorced/widowed	2 (6)
Education, y	
<12	6 (19)
≥12	26 (81)
Ethnicity	
White	32 (100)
Other	0
Fitzpatrick skin type	
I	2 (6)
II	5 (16)
III	15 (47)
IV	10 (31)
V	0
Filler type injection area	
AG only/radix-nasal spine	0
HA only/tip-supratip	0
Both	32 (100)

Table 2. Clinical Evaluation Scores Showing the Patient Satisfaction Scores and GAIS Results Showing Two Independent Plastic Surgeons' Objective Scores after Injection

Patient No	Clinical Evaluation Scores (0–10)		GAIS (1–5)	
	0: Not satisfied with the results, 10: Very satisfied		1: Best result, 5: Worst result	
	After Injection	Two Weeks Later	Plastic Surgeon A	Plastic Surgeon B
	Mean score ± SD: 9.09 ± 0.93	Mean score ± SD: 9.00 ± 0.88	Mean score ± SD: 1.72 ± 0.58	Mean score ± SD: 1.69 ± 0.59
	Median: 9.00	Median: 9.00	Median: 2.00	Median: 2.00
Min–max: 7–10	Min–max: 7–10	Min–max: 1–3	Min–max: 1–3	
1	9	9	2	2
2	9	9	2	2
3	8	8	3	2
4	10	9	1	2
5	10	10	2	2
6	10	10	2	2
7	9	9	1	1
8	9	9	2	1
9	7	7	3	3
10	10	10	1	1
11	10	9	1	1
12	7	7	2	3
13	9	9	2	2
14	7	7	2	2
15	10	9	1	1
16	9	9	1	1
17	10	10	2	2
18	9	9	2	2
19	10	10	2	2
20	8	8	2	2
21	9	9	1	1
22	9	9	2	2
23	9	9	2	2
24	10	10	1	1
25	9	9	2	2
26	10	10	1	1
27	9	9	2	2
28	10	10	2	1
29	8	8	2	2
30	9	9	1	1
31	9	9	2	2
32	10	10	1	1

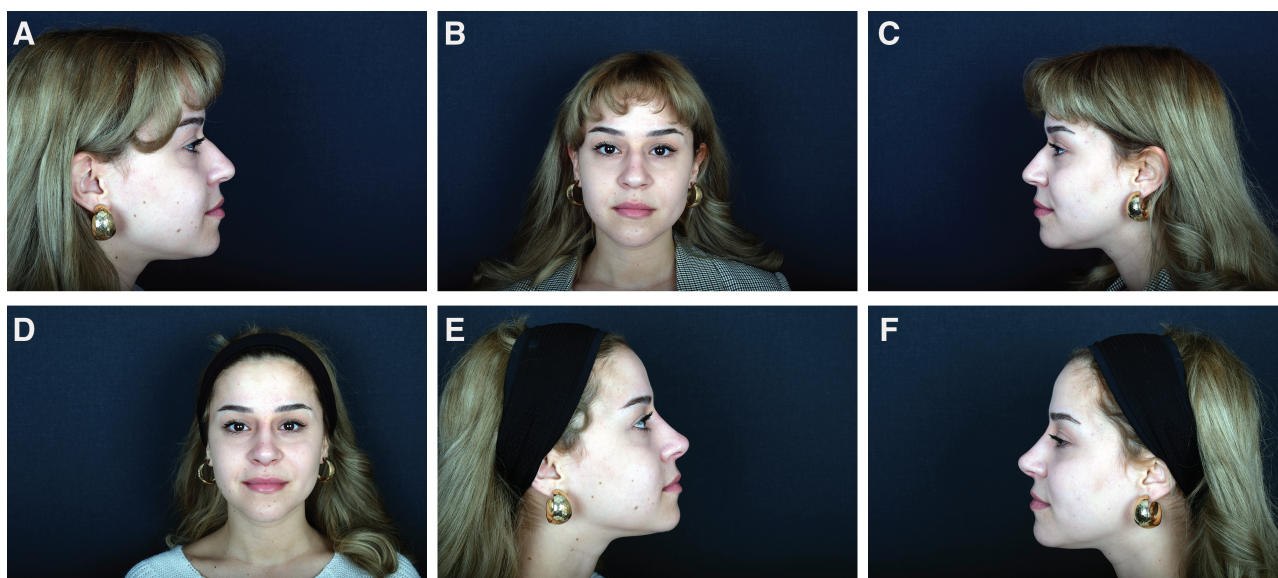


Fig. 2. Preprocedure (A–C) and 6 months (D–F) postprocedure results of a 22-year-old female patient after 3.5% Algeness treatment.

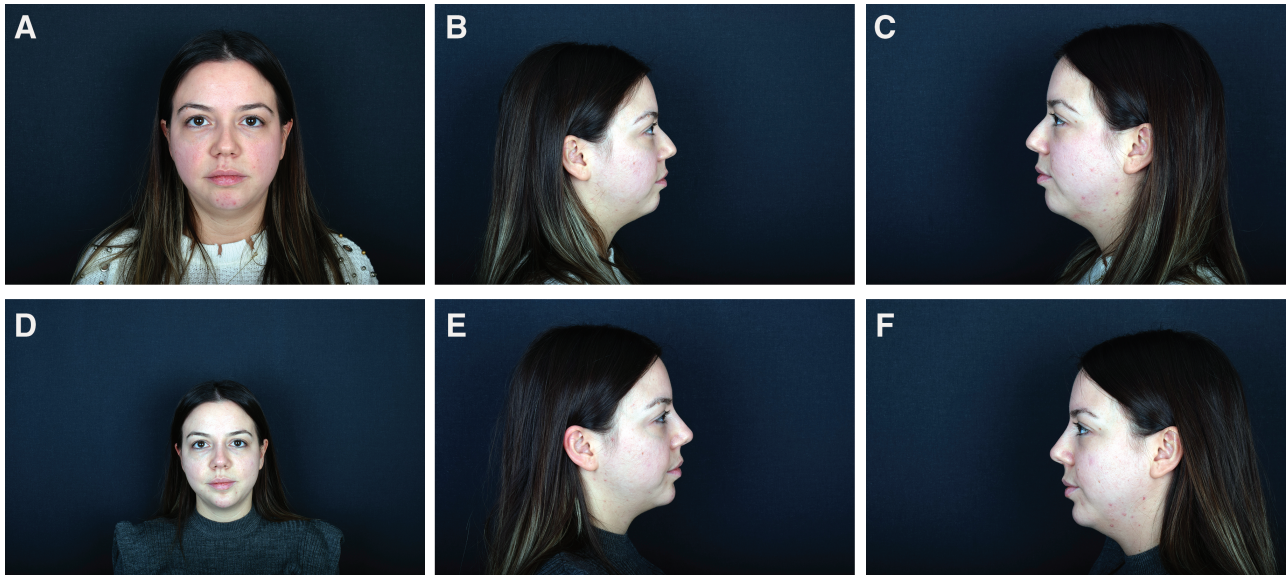


Fig. 3. Preprocedure (A–C) and 6 months (D–F) postprocedure results of a 31-year-old patient after 3.5% Algeness treatment.



Fig. 4. Preprocedure (A–C) and 10 months (D–F) postprocedure results of a 28-year-old male patient after 3.5% Algeness treatment.

can be used in the case of any accidental intravascular injection.²⁸ No complications related to intravascular injection with AG have been reported to date. Although treatments such as saline and hyaluronidase are recommended in the literature in a possible case, we argue that the protocol for particulate soft-tissue fillers should be applied in general.²⁹

Complications and major adverse events such as abscess, inflammatory nodules, and granulomas can rarely be seen after injectables, but have not been reported in the literature following AG injections yet.⁸ Lumps may also occur if big bolus injection is applied due to the low migration effect of AG. It is important to pay attention to the application method during the procedure in this respect.

CONCLUSIONS

Given its structural properties, it would be a mistake to assume that a single type of filler fits perfectly to each anatomical region of the nose in nonsurgical rhinoplasty procedures. Therefore, we used two different structural fillers to different regions of the nose according to their advantages and disadvantages. In the radix and the nasal spine, we need a filler suitable for supraperiosteal application that does not expand by creating edema, does not have any migration, has a high G-prime and thereby gives more precise contour. In the tip and the supratip area, we need a filler that can be applied intradermally which can expand the skin with a small amount of filler and does not create any lump formations.

After all, according to this study, clinical results of the association of two different types of fillers were very good, they did not cause any significant adverse events, and the patients were satisfied. To our knowledge, this is the first study adopting the understanding of a hybrid approach with a new AG and HA filler in different anatomical locations for nonsurgical correction of the nose. We can conclude that AG and HA fillers can be used successfully with a hybrid combination, and this concept represents a safe and convenient option for nonsurgical rhinoplasty procedures. However, randomized controlled trials are necessary to prove the efficacy.

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