Acta Scientific Otolaryngology

Volume 3 Issue 11 November 2021

Mini Review

Current Considerations for Injectable Nasal Fillers

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Received: April 26, 2021

Published: November 29, 2021

Abstract

Injectable soft tissue filler procedures continue to grow in popularity as a minimally invasive option to address facial volume loss, rhytids and contour deformities. Nonsurgical, injectable, or liquid rhinoplasty refers to the use of injectable filler to augment limited areas of the nose, improving nasal appearance or function. Hyaluronic acid and calcium hydroxylapatite are the most commonly used nasal filler materials, given their rheologic properties, lifting capacity, biocompatibility, and longevity. Despite a growing body of literature describing how to safely perform nonsurgical rhinoplasty, complications including vascular occlusion, skin necrosis and blindness have been well described. This article reviews the indications for nonsurgical rhinoplasty, considerations when choosing a filler product, pertinent anatomy, pearls for injection technique and provides an overview of known complications.

Keywords: Injectable Filler; Soft Tissue Filler; Non-Surgical Rhinoplasty; Liquid Rhinoplasty; Hyaluronic Acid

Abbreviations

HA: Hyaluronic Acid; CaHA: Calcium Hydroxylapatite; SMAS: Superficial Musculoaponeurotic System

Introduction

Injectable fillers are widely used to address areas of facial volume loss, rhytids, and contour deformities. Dermal fillers have been used in facial rejuvenation since the introduction of bovine collagen products in the early 1980s [1]. Since then, many soft tissue filler materials have become available on the market, including hyaluronic acid (HA), calcium hydroxylapatite (CaHA), poly-l-lactic acid, polymethyl methacrylate and silicone [2]. The varying physicochemical properties of these products can help predict how they will behave *in vivo*.

Nonsurgical, injectable, or liquid rhinoplasty refers to the use of temporary soft tissue filler to augment limited areas of the nose to improve nasal appearance or function. The use of soft tissue fillers has grown immensely over the past two decades, from an estimated 652,885 procedures in 2000, to an estimated 2,721,469 in 2019 [3,4]. Nonsurgical rhinoplasty has grown in popularity since its conceptualization in 2006 [5]. The goal of this mini-review is to summarize the commercially available soft tissue filler products commonly used in the nose, their indications, injection techniques, and discuss known complications of nasal fillers.

Indications

Injectable rhinoplasty is a minimally invasive option for patients who are medically unsuitable for surgery, or who are reluctant to take on the cost, downtime or risks of a surgical procedure. The

cosmetic corrections achievable via injectable rhinoplasty can be conceptualized as similar to those achieved by surgical onlay grafting or camouflaging (radix graft, tip graft, etc.), rather than surgical reduction or structural grafting. In addition, it is important to note that while nasal filler can address mild to moderate contour deformities, major changes in contour may not be safely and easily achievable.

Cosmetic indications for nonsurgical rhinoplasty include [6-10]:

- Deep radix
- Dorsal hump camouflage
- Crooked nose camouflage (e.g. upper or middle third asymmetry)
- Post-rhinoplasty contour correction
- Desire for increased tip projection or definition
- Correction of nasal tip ptosis
- Alar rim irregularities
- Alar base deficiency.

A review of 5000 patients undergoing nonsurgical rhinoplasty with a single plastic surgeon suggests that among these, dorsal hump correction is the most common indication, followed by post-surgical correction and tip ptosis [6]. While functional nonsurgical rhinoplasty may be less commonly performed, injectable spreader grafts to address internal nasal valve collapse have been described [11]. Dermal filler injection in the scroll and along the nasal sidewalls has also been described to address dynamic nasal valve collapse [12].

Nasal filler selection

Of the 2.7 million soft tissue injectable procedures performed in 2019, HA injections comprised 79.5%, CaHA 8.1%, polylactic acid 4.4%, autologous fat (1.7%) and polymethyl-methacrylate microspheres (< 1%). Injectable rhinoplasty has been well described using both HA and CaHA fillers [6,7]. A number of products are available in each of these families, each with distinct rheological properties that determine the behavior of these materials *in-vivo*. A brief discussion of several clinically relevant rheological properties follows.

Filler rheology

Creating definition in a thick-skinned nasal tip or lifting the thick soft tissue at the radix may more easily be achieved using firmer gels that resist deformation, in the manner of peanut butter, rather than products that readily integrate into the surrounding tissues, in the manner of maple syrup. The rheologic terms G', G'', G* and η* help to describe how a filler will behave *in-vivo* and are discussed below.

A gel's elastic modulus or G' is a measure of the product's ability to resist deformation [5]. G' can also be thought of as the amount of energy stored by a gel [8]. In the context of HA fillers, the G' is dependent on several factors, including the density of HA crosslinking, the gel's HA concentration, and the presence of unbound HA within the gel [12]. A product with higher G' is considered firmer than one with a low G', and generally provides more "lift" when deposited into soft tissue. However, because high G' products resist deformation, they may feel stiffer within the tissues [9].

G'' denotes a gel's viscous modiolus, a measure of the gel's ability to dissipate energy upon application of a force. A higher G'' gel is thicker and requires a greater extrusion force to be expressed through a needle (e.g. peanut butter, rather than honey). Together, G'' and G' define the complex modulus, or G*, which represents a gel's total resistance to deformation, as determined by this formula [13]:

$G^* = (\text{square root of } (G')^2 + (G'')^2)$.

Soft tissue fillers are viscoelastic, though the elastic component is more significant. Because the G' value is much larger than that of G'', and G* and G' are almost identical. G' is more widely reported and may be considered a proxy for G*.

The complex viscosity η* is a measure of the gel's total resistance to flow. It can be calculated at any given angular frequency (ω) by the following: $\eta^* = G^*/\omega$. A lower viscosity suggests that a gel may experience more dispersion into the surrounding tissues, limiting the "lift" generated within a well-defined area. Table 1 lists the G' and η* of several commercially available products, with a much higher G' and η* seen in the CaHA product Radiesse®, compared to the HA products.

The swelling factor describes a gel's ability to take up fluid *in-vitro* while maintaining a single phase [11,12,14]. Unlike aqueous solutions, gels uptake water to a finite degree before phase separation, or separation of the particulate from the solution occurs. The swelling factor thus indicates a gel's water saturation status. When

Filler Type	Commercial Name	Elasticity G' (Pa)	Viscosity η*, cPA
HA	Restylane® Lyft	541	124,950
	Restylane®	513	119,180
	Juvéderm® Voluma™	274	62,902
	Juvéderm® Ultra Plus	75	17,699
	Juvéderm® Ultra	28	7,307
	Boletero Balance®	38.7	10,453
CaHa	Radiesse®	1407	349,830

Table 1: Viscoelastic properties of various hyaluronic acid and calcium hydroxylapatite formulations. Adapted from Sundaram H, Voigts B, Beer K, Meland M. Comparison of the rheological properties of viscosity and elasticity in two categories of soft tissue fillers: calcium hydroxylapatite and hyaluronic acid. Dermatologic Surg 2010; 36 (Suppl 3):1859-1865.

Values are reported at 0.7Hz.

nearly saturated and near equilibrium, a gel is expected to take up less water once injected into tissues, compared with unsaturated gels below equilibrium.

In the context of HA fillers, the swelling factor is inversely proportional to the term c_{min}, which is equivalent to the HA concentration of a fully swollen gel without any unbound HA molecule. Therefore, a low c_{min} reflects a higher swelling factor and vice versa.

Swelling factor = $1/c_{min}$.

In general, the swelling factor is inversely related to G' [5,12], as highly crosslinked gels with a higher HA concentration are limited in their ability to incorporate water molecules, since the HA molecules are closely associated with one another [11].

While increased hydration may be desirable in some areas such as the lips, this may be problematic in injectable rhinoplasty. For example, attempting to improve tip definition with a product that takes up significant water may cause a more amorphous tip.

In addition to rheology, other considerations when choosing a nasal filler include the biocompatibility, longevity, and reversibility of the product. Hyaluronic acid products are easily broken down by commercially available hyaluronidase and are thus reversible in the event of unsatisfactory cosmetic outcome or vascular compromise. CaHa products on the other hand are not easily dissolved. CaHa may offer a longer effect at 12 - 18 months, compared to the 6 - 12 months that HA products provide.

Silicone injectable rhinoplasty has fallen out of favor due to the high rates of infection, hematoma, telangiectasia, as well as foreign body granuloma formation [13-15].

Pertinent anatomy

Knowledge of and attention to the relevant anatomy is crucial for safe and effective injection rhinoplasty. Firstly, it is important to consider the skin-soft tissue envelope. The skin-soft tissue envelope is comprised of the skin, deep to which is the superficial fat, the nasal superficial musculoaponeurotic system (SMAS), loose areolar tissue, and the perichondrium or periosteum. The majority of blood vessels supplying the external nasal skin run through the superficial fat or in the nasal SMAS [16]. Since filler is often injected in the avascular supraperiosteal or supraperichondrial plane, it is inherently placed deep to the skin-soft tissue envelope. Small contour changes may be masked by thick skin, limiting the aesthetic change achieved with a given amount of filler. In addition, patients with thicker skin-soft tissue envelopes may experience more significant post-injection edema.

The vascular supply to the external nasal skin has contributions from both the internal carotid and external carotid arteries. The ophthalmic artery is a branch of the internal carotid artery, which gives rise to the anterior ethmoid and the dorsal nasal arteries in the upper portion of nose. The facial artery, a branch of the external carotid system, gives rise to the angular and superior labial arteries, which supply the lower part of the nose. The angular and superior labial arteries give off the lateral nasal artery and columellar artery respectively, to supply the nasal tip [17]. In the middle third of the nose, the dorsal nasal artery anastomoses with branches of the facial artery. Compression of these vessels or intravascular injection during nonsurgical rhinoplasty can cause devasting complications, which will be discussed herein. Finally, anatomy may be altered in post-surgical rhinoplasty patients, further increasing the complexity of injectable rhinoplasty.

Pearls for injection

Principles of safe injection technique center around avoiding intravascular injection and extrinsic vessel compression, to prevent

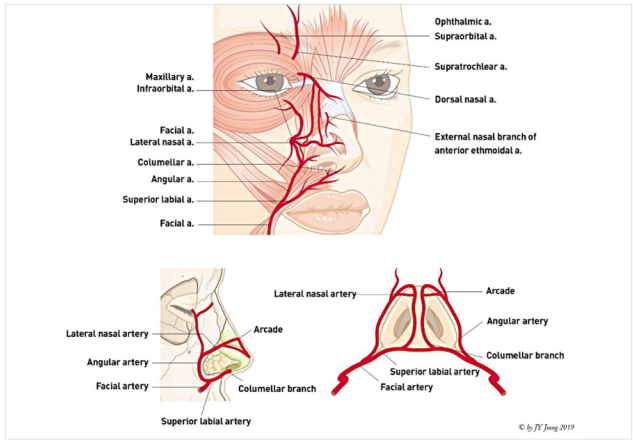

Figure: Reproduced from: Kim, Taek Kyun, and Jae Yong Jeong. "Surgical anatomy for Asian rhinoplasty." *Archives of craniofacial surgery* vol. 20,3 (2019): 147-157. doi:10.7181/acfs.2019.00290 and used under a Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/).

subsequent tissue necrosis or blindness. A number of factors can influence the procedure's inherent risk, including patient anatomy, tissue plane of injection, injection location, and technique. Given the location of the nasal vasculature in the superficial fat and nasal SMAS planes [16], injection into the supraperiosteal/supraperichondrial avascular plane is considered relatively safe. It is possible however, to insert the tip of a needle through a blood vessel before entering the supraperiosteal/supraperichondrial plane and in these instances, filler can enter the vessel upon withdrawal of the needle. Given the locations of the paired dorsal and lateral nasal arteries, injection in the midline along the dorsum and midvault can help to avoid intravascular injection.

Even when placed extraluminally, filler boluses can limit tissue perfusion if the pressure of injection exceeds nasal arterial blood pressure. Slow injection of small volume aliquots at low pressure can help to limit extravascular ischemic complications [18]. Small syringes and blunt cannulas have also been suggested, as some authors feel they decrease opportunity for vessel penetration [18]. Additionally, it is critical for injectors to continuously reassess the color/pallor of the nasal skin-soft tissue envelope as well as the of depth of injection over the course of a procedure. The use of a local anesthetic containing epinephrine can cause pallor due to epinephrine induced vasoconstriction, prior to injection of dermal filler. Vasoconstriction induced vasoconstriction resolves however, within 14 - 53 minutes with duration increasing in a concentration dependent manner [19], is painless and occurs in the region immediately adjacent to injection. Arterial occlusion typically causes immediate pain with persistent pallor, sometimes in a geographic region. Venous occlusion may be associated the development of a dark or violaceous discoloration of the affected area and accompanied by dull or delayed pain. The symptoms associated with venous occlusion may be incorrectly attributed to post-procedural bruising, but disproportionately persistent or severe pain should prompt further consideration.

Complications

Complication rates in recent reviews of nonsurgical rhinoplasty are in the range of 1.63 to 7.6% [20-22]. Bruising was the most commonly reported complication, with an incidence of 1.58% [21]. Hematoma, telangiectasia, infection, subcutaneous nodule formation were also reported [20,21]. Skin necrosis and vision changes are among the most severe complications of nonsurgical rhinoplasty and are discussed below in relation to vascular compromise.

Vascular compromise can occur as a result of extraluminal vessel compression, intravascular embolization or vascular spasm [23]. In the short-term, vascular occlusion can cause pain, edema and erythema, though long term complications include blindness, dermal necrosis, scarring, hypo or hyperpigmentation and contour deformity [20,22]. In Rivkin's recent review of 2488 nonsurgical rhinoplasty procedures, the rate of serious adverse events (ischemia and necrosis) was 0.2% [22]. The anastomoses between the dorsal nasal artery and branches of the facial artery in the middle third of the nose provide routes for emboli to affect both the internal and external carotid systems, potentially affecting multiple angiosomes.

Rivkin stratified his rate of adverse events by patients' history of surgical rhinoplasty and found that previous surgical rhinoplasty was significantly more likely to experience adverse events at a rate of 10.8%, compared to 7.4% without prior surgery [22]. When examined with attention to injection site, the nasal tip and

sidewall were more likely to result in an adverse event compared to the other areas of the nose (e.g. dorsum, radix, and ala), and this applied to both postsurgical and non-surgical patients [22]. He postulates that the adverse events in the nasal tip were secondary to a compartment syndrome rather than embolic event due to the very small nature of the tip vessels. The sidewall adverse events however, may have been embolic in nature given the larger caliber of the angular artery and its branches, and the relative ease of puncture while injecting the nasal sidewall. Rivkin also examines his adverse event rates by filler, having used CaHA alone or in combination with a HA filler (58.3% of all cases), as well as a HA filler alone (19%), and PMMA (18.6%) [22]. He describes the use of CaHA in combination with an HA filler for patients requiring the most augmentation or definition, which required more needle punctures resulting in increased bruising, as well as greater skin stretch leading to increased incidence of erythema, and larger volumes injected, leading to an increased incidence of ischemia [22]. Of interest, both Williams [20] and DeVictor [21] found higher complication rates when CaHA was used for nonsurgical rhinoplasty, compared to HA.

Occlusion of the central retinal artery or its branches is a rare but devastating complication after dermal filler. It can occur if a distal branch of the ophthalmic artery, such as the dorsal nasal artery, is pierced and high force of injection causes retrograde flow of a filler embolus into the central retinal artery or its branches [24]. Painless vision loss in the affected eye can occur seconds after injection. Central retinal artery occlusion of greater than 60 - 90 minutes duration can cause irreversible blindness, and emergent treatment should initiated be taken as soon as visual loss is recognized [25]. While the treatment for central artery occlusion is outside the scope of this article, multiple expert consensus statements exist in the literature [24,26].

Summary

Rheology, biocompatibility, longevity, and reversibility are important factors for consideration when choosing a nasal filler product. Hyaluronic acid and calcium hydroxylapatite are the most commonly used filler materials for injectable rhinoplasty at this time. The cosmetic corrections achievable by injectable rhinoplasty can be conceptualized as similar to those achieved by surgical onlay grafting or camouflaging (radix graft, tip graft, etc.), rather than surgical reduction or structural grafting. Rare but devasting complications of injectable rhinoplasty include vision loss and irreversible blindness. Other early complications include ecchymosis, edema, pain/tenderness, erythema, infection, and local tissue ischemia. Delayed complications include filler migration, nodules, foreign body granuloma, biofilm, tissue necrosis and contour irregularities. An understanding of nasal anatomy with attention to vascular supply and injection technique can help to minimize the incidence of complications.

Conflict of Interest

The authors have no conflict of interest to declare.

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