

Adverse Effects When Injecting Facial Fillers

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Facial soft-tissue augmentation has become ubiquitous in cosmetic dermatology. In the appropriate patient and with appropriate training, fillers can temporarily eliminate rhytides, creases, and defects, thereby producing a rejuvenated appearance. Yet, even in the most experienced injectors, there can be complications. These adverse effects can be divided into early and late and range from bruising to necrosis. Understanding the anatomy, limitations of the filler and proper technique can reduce the risk of adverse effects. When a complication occurs, the practitioner should understand how to manage them from observation to surgical intervention.

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With the recognition of the importance of volume in facial rejuvenation, injectable fillers have become a very important option in the dermatologic surgeon's armamentarium.¹ In experienced hands, fillers are safe and effective.² Yet, fillers are implants and essentially foreign bodies that may remain in some form for up to several years. Fillers need to be injected at a certain level of the skin. However, this is a blind procedure, as the physician is unable to see exactly where the filler is placed. With these characteristics, injectable fillers (which often are viewed as an entry procedure in one's practice) have the potential for a myriad of complications. Adverse effects are not uncommon. In one study of 286 patients injected with hyaluronic acid gel, there was a complication rate of approximately 5%.³

Anatomy and High-Risk Regions

Although injectable fillers theoretically can be used in any anatomic region, they are most commonly used for filling facial lines, depressions, and augmenting aging cosmetic units. The skin thickness also varies dramatically depending on the cosmetic subunit. Although the rich network of blood vessels may be a very favorable feature for other procedures such as rhytidectomies, it can increase the chance of bruising

and hematomas when performing injections. More serious complications include emboli and resulting necrosis. There have been several reported cases of necrosis when injecting in the glabellar region.⁴⁻⁷ Although the glabella must be respected as a high-risk area when injecting, necrosis also may occur in common injection sites. Cases of necrosis after performing hyaluronic acid injections in the nasolabial folds were recently presented.⁸

The facial cosmetic units also are characterized by the differences in skin thickness. There are wide variations of skin thickness and texture within the cosmetic units. There are 3 central facial cosmetic units in the "I" zone that are particularly susceptible to complications. A tell-tale sign of aging is in the periorbital region where there is a loss of volume and subsequent hollowing of the eyes. This depletion of soft tissue leads to the "double bubble"—the loss of a smooth continuous contour from the lower eyelid to cheek. The eyelids and periorbita have a very thin dermis, and injections into this layer will inevitably lead to lumpiness and potential granulomas whether the practitioner is injecting hyaluronic acid, calcium hydroxylapatite (Radiesse, Bioform Medical, San Mateo, CA) or poly-l-lactic acid (Sculptra, Dermik Esthetics, Berwyn, PA).

Because of the variability of skin thickness in different anatomic facial regions, soft-tissue filler placement in the periorbital skin is not the only complicated site in the treatment of aging facial skin. Augmentation of the nose can also be quite challenging and lead to a higher rate of complications. The skin of the nasal dorsum is usually very thin in contrast to the sebaceous quality of the tip and supratip subunits. Injecting in the nasal dorsum for either augmentation or making existing humps less noticeable requires injections deeper than the conventional technique. Injections into the

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dermis in this cosmetic subunit will increase the risk of lumpiness and nodules. Similarly, the lip is another anatomic area which can have poor outcomes. The lip's thin mucosa is very unforgiving if the filler is too thick or the injection technique is not meticulous. Although the marionette lines do not share the same risks as these other sites, because they are adjacent to the commissure, the lip can become distorted. Augmenting the chin with calcium hydroxylapatite or fat could potentially lead to vascular compromise if too much of the product is injected at one time compressing the blood vessels aside from enlarging the chin to an abnormal degree.

Understanding the Fillers

Despite media hype, there is not one filler that satisfies all sites or a perfect injectable. Rather, each filler has a specific niche. It is important to understand where fillers should and should not be used—or at least with extreme caution—to decrease the risk of adverse events. Understanding the depth in which to inject each implant is crucial. If a filler such as calcium hydroxylapatite is injected into the papillary dermis, it will increase the risk of superficial papules. Fillers such as human collagen and the medium life hyaluronic acids such as Restylane (Medicis, Inc, Scottsdale, AZ) and Juvederm Ultra (24HV; Allergan, Inc, Irvine, CA) if injected with the proper technique are at lower risk, though in some regions may not provide a satisfactory result because of their lack of volume. While more viscous fillers such as calcium hydroxylapatite, poly-L-lactic acid and fat can be very versatile, they will have a higher complication rate if injected into certain regions such as the lip.

Generally, “lighter” products such as the human collagens and the medium hyaluronic acids such as Restylane and Juvederm Ultra are very appropriate for the lips, marionette lines, nasolabial folds, fine rhytides, glabellar folds, the periorbital and for filling acne scars. The “heavier” injectables such as calcium hydroxylapatite, cross linked hyaluronic acid (Perlane, Medicis, Scottsdale, AZ), and fat are excellent for the nasolabial folds, marionette lines, prejowl sulcus cheeks, the temporal fossa and scars. They need to be used judiciously in the periorbital to avoid lumpiness, but can be very effectively with the right volumes and depth of placement. These “heavier” products are usually avoided in the glabellar folds. They can be excellent for augmenting specific structures such as the nose and chin, though fat transplants may lead to lumpiness in these areas. Essentially, the heavier implants are best for pan-facial rejuvenation.

Technique Considerations

As with other cutaneous procedures, it is necessary to receive adequate training before using soft-tissue augmentation agents. In our opinion, physician injectors should first be made to demonstrate a detailed knowledge of anatomy and possible adverse events (such as sensitivity, infection and necrosis) through passing an American Board of Medical Specialties examination in one of the CORE esthetic specialties after residency training in one of these disciplines.

Training for implant injections can be more complex given that, if there is an adverse effect, in many instances, it (or part) will remain for several months. Minor interventions may not work or be feasible, complications can be devastating to the patient. Moreover, although a practitioner may be very competent in injecting a certain cosmetic unit, if he or she chooses to offer other more complex sites such as the periorbital, then training for this site should be undertaken. Aside from being intimately aware of the particular product's limitations (such as reading articles in peer reviewed journals), observation and practical experience are the keys to excellence. Initially observing an experienced injector in interactive sessions, and then practicing on a cadaver head will lay a foundation.

For the first several injections, it is wise to have your injections proctored by an experienced injector. Although this scrutiny may cause anxiety in some novices, the advantage is the correction of technique so as not to develop bad habits that would lead to complications. When finally injecting on one's own, the initial patients should be those with which the practitioner already has a bond. Some physicians will decrease their fee for the first several patients as well as place on the consent that the patient understands that the practitioner has limited experience with this procedure. While these last two tactics will not necessarily decrease the legal risk of a complication, the patient may be more understanding should one occur. It is important to maintain one's skills. For less-common areas such as the chin and nose, the practitioner may want to inject staff or offer discounts for established patient who has the appropriate condition.

Technically, it is most important what depth to place a specific implant. In brief, human collagen should be placed in the mid-dermis. Medium length hyaluronic acid products such as Juvederm and Restylane should be placed in the deep dermis.⁹ Calcium hydroxylapatite is injected at the dermal-subcutaneous border.^{10,11} Poly-L-lactic acid and fat are injected into the subcutis.¹² Injecting a filler too superficially will lead to lumpiness, nodules and an unsatisfactory result. In many instances, it is impossible to distinguish the mid dermis and the deep dermis. Generally, it is better to err on placing the filler deeper. The downside of this deeper placement is that the augmentation effect may not be as apparent, though it may last longer given less mobility.

In terms of specific injection technique such as multiple serial puncture versus linear threading, there have been no studies to suggest that one type of placement is superior. Multiple puncture is somewhat easier to control placement, though it can lead to unevenness unless there is overlap. When using this technique, the practitioner must also remember to reduce pressure on the plunger as the needle is exiting to avoid superficial deposition of filler. The linear threading technique tends to require more experience, and can result in too much product in one area. Though most practitioners ultimately prefer this linear threading technique, most injectors typically utilize some combination of both methods.

Patient Assessment and Education

As with any other aspect of medicine, and in particular pertaining to cosmetic surgery, a strong patient-physician bond is important when administering fillers. In the best situation, the patient will have had other procedures performed at the office and a trust established with the physician. In the consultation, the patient's esthetic concerns need to be addressed in a detailed manner, since a filler may not be the solution to her/his concerns and another procedure may be a better option. The patient's expectations need to be realistic in terms of the specific effect of the filler and the overall facial effect. A detailed medical history should be taken. Patients with active infections should delay cosmetic procedures. Aspirin and nonsteroidals or coumadin need to be stopped before the procedure; if this is not possible, the patient should be made aware of the increased risk of bleeding and this should be written into the consent. While immunosuppression is not a contraindication for fillers, the higher risk of infection should be discussed. In those patients with immunologic diseases such as lupus or scleroderma, it is best to discuss with the patient's medical dermatologist or rheumatologist before proceeding.

The approximate duration of the fillers need to be discussed. The patient should be given a choice of different fillers, the benefits and risks of each, and should participate in the decision-making process. The use of anesthesia should be discussed, as well as the amount of discomfort the patient would be expected to have both during and after the procedure. For instance, the injection of calcium hydroxylapatite may cause a transient "achiness." Detailed postoperative care and potential minor adverse effects need to be reviewed. Of course, the risk of major and delayed adverse effects need to be discussed in a manner which educates the patient rather than creating additional anxiety. All potential adverse effects should be listed in the informed consent and reviewed with the patient before injection.

Complications

Early Minor

Despite the best intentions and technique, there can still be minor complications such as bruising, swelling, tenderness, and skin discoloration. Bruising can be immediate or within a few hours. Occasionally, it may reveal itself the next morning. Ecchymosis is almost invariably minor, and generally limited to around the injection site. If a patient is on some form of blood thinning medications or some vitamin supplements (including vitamin E, ginseng, garlic, ginger, ginkgo, etc.), bruising can be quite profound. In some instances, ecchymosis covers the majority of the facial anatomy below the injection site and may require several weeks to fully resolve.

Anecdotally, homeopathic medications such as echinacea have been reported to reduce bruising. However, there have

been no studies showing a difference in postinjection bruising in those who taking this medication. Ultimately, excellent technique will decrease the risk of bruising. Interestingly, the fanning technique which is favored by many practitioners has been reported to increase the likelihood of bleeding. Because injectables are a blind technique, even experienced individuals may pierce a small vessel and cause ecchymosis.

Transient swelling may occur simply because of the irritation of placing a foreign implant within the skin or because of an indelicate technique. This swelling may last from 24 to 72 hours. Similarly, temporary tenderness may occur because of the needle trauma or because of the physical imposition and subsequent volume displacement on the skin from an implant. Generally, both swelling and tenderness will more pronounced in the semi permanent fillers compared with the shorter-acting injectables. This postinjection "ache" most likely occurs due to volume displacement of the stretching of cutaneous nerves. Skin discoloration, particularly erythema along the injection site has been documented both in the hyaluronic acids and in calcium hydroxylapatite.^{3,13} Although it is unlikely to be a hypersensitivity reaction, there may be mast cell release contributing to this discoloration. Fortunately, in the vast majority of patients, the erythema will resolve in 2 to 3 days.

Major

Because facial augmentation with injectables is a cosmetic procedure whose purpose is to improve appearance, any sequelae that actually worsens the patient's cosmesis is a significant complication. Many patients have asymmetry at baseline. While this quality can be corrected with fillers, it should be discussed during the consultation, and the patient should be aware that he/she may still have some asymmetry after the procedure. We recommend photographs be taken for documentation both before and after the procedure.

Gross unevenness after soft-tissue augmentation is certainly not acceptable. Lumpiness may resolve with massage. However with semipermanent fillers injected too superficially, the lumpiness may remain for several months (Fig. 1).



Figure 1 Lumpiness and deposits in the infraorbital region after a Restylane injection that was too superficial. (Color version of figure is available online.)

Although physicians strive to achieve a full correction, to overcorrect with a long-lasting filler is problematic. This result could remain for several months and be very difficult to disguise.

Hematoma is an uncommon occurrence, but it can result from the inadvertent laceration of small facial blood vessels. Because of the supratrochlear artery and anastomosing blood vessels in the glabellar region, there may be a higher risk for hematoma when injecting frown lines. Immediate hypersensitivity is rare, and has been associated with bovine collagen. Anaphylaxis could occur secondary to preservatives.¹⁴ Although infection is rare, the trauma of injection could lead to an HSV infection and potential long term pigmentary changes or small punctuate scars (Fig. 2).

Delayed Complications

Minor

Occasionally, delayed small bumps may occur. This complication can occur with any filler, but is more likely with implants that need to be injected at least in the mid dermis or deeper such as the hyaluronic acid gels, calcium hydroxylapatite or poly-L-lactic acid. Their etiology is unclear. Most commonly, it again may be due to a portion of an injection which was too superficial. These papules may have a bluish-tint known from the Tyndall effect of placing this foreign gel in a superficial plane (Fig. 3).¹⁵ Although delayed hypersensitivity reactions can occur in implants with animal particles, it is exceedingly rare in those implants with nonanimal derivatives to cause hypersensitivity reactions. Initially, hyaluronic acid implants performed outside the United States seemed to have higher immunogenicity risks, but this was most likely due to higher protein contents as well as impurities, and currently purification techniques have virtually eliminated this complication.

Major

True granulomas are rare. They occur in approximately 0.1% of the patient population.¹⁶ The majority will result from



Figure 2 Herpes simplex virus blisters and ulceration after soft-tissue augmentation of the lips. (Color version of figure is available online.)



Figure 3 The Tyndall effect—a bluish hue from a Restylane injection into the papillary dermis. (Color version of figure is available online.)

injections of semipermanent and permanent fillers. Granulomas, which are the body's response to a foreign material, will present most commonly as dermal nodules with mild erythema. They may appear singly or in small clusters. They may or may not be tender. Though they usually will appear within the first 6 months after injection, delayed granulomas fourteen months after injecting polymethylmethacrylate microspheres have been reported.¹⁷ In most patients, they are fairly obvious and create significant anxiety.

Infection can be an early complication and is most likely due to common skin pathogens such as staphylococcus aureus. However, when infection arises later, they may be due to other less common bacteria. In contrast to granulomas, they will appear as fluctuant nodules, with more surrounding erythema and warmth and tenderness. The patient may also have a fever. Similar to other cosmetic procedures such as liposuction, mycobacteria may be the causative agent in delayed filler infections. Sterile abscesses may also occur without evidence of bacteria (Fig. 4).

Migration with permanent implants such as expanded polytetrafluorethylene have been well documented.¹⁸ It is



Figure 4 Sterile abscesses after a Restylane injection. Three cultures were negative. (Color version of figure is available online.)

much less frequent with temporary fillers which are reabsorbed. There is a potential higher risk with semipermanent and permanent implants such as calcium hydroxylapatite and silicone. Yet, in 3 studies with calcium hydroxylapatite there have not been any cases of migration.^{13,19,20} But some reports discuss migration of calcium hydroxylapatite superficially in the lip leading to the appearance of “popcorn lip.” With the microdroplet technique for silicone placement, migration is much less likely. Migration can occur up to several years after the injection. An infection or delayed granulomatous reaction may trigger migration. In some patients who have dramatic changes in laxity and elastosis due to normal facial aging, it may appear that the implant has migrated when in fact the facial anatomy has changed somewhat over time.

Management of Complications

Avoidance

The best way to manage complications is to avoid them. Understanding which filler is appropriate for each anatomic site and its particular limitations is fundamental in avoiding adverse effects. For example, while calcium hydroxylapatite is a very versatile implant, its use for lip augmentation carries a risk of lumpiness and nodularity. While this effect will slowly diminish, management can be challenging since a corticosteroid injection into the lip to decrease the nodule also carries a risk of atrophy. This can lead to a “snowballing” effect of complications which can lead to a permanent lip deformity and a very unhappy patient.

Producing consistently excellent results and avoiding poor outcomes and complications begins before the actual injection. Marking patients before injection is a good habit which will ensure reproducibility. Expressions can change or the lighting angle may alter the appearance of the rhytide or defect.

Anesthesia, including nerve blocks, can potentially distort the site of injection due to the volume. While nerve blocks are certainly acceptable before filler injection, this type of anesthetic does not constrict local blood vessels. When injecting the nasolabial folds, a direct infiltration of 1 mL of 1% lidocaine with 1/100,000 epinephrine along the folds will constrict the blood vessels and decrease the risk of piercing a blood vessel and causing ecchymosis or inadvertent injection of the substance into the vessel. While there is initial distortion of the site, this dissipates in 15 minutes while the practitioner is treating other patients. In addition, because a smaller anatomic region will be “frozen,” the patient will generally be happier with the overall treatment.

Evaluation

When a patient presents with an undesired effect, they should be seen promptly. It is important to explain that an adverse effect has occurred and to have a plan of action. The patient needs to be informed that the treatment plan may require multiple sessions. In addition, a discussion regarding the potential for any permanent blemishes from these interventions (such as a scar) should be had. Initially, the physi-

cian should determine whether this adverse effect will potentially resolve on its own and whether only reassurance is only necessary or whether it requires intervention. Yet, even adverse effects that diminish over a relatively short period of time may be unacceptable to the patient. For instance, superficial beading will generally resolve over the course of a month, but it can be very difficult to camouflage with cover-up. If there is an irregularity due to a semipermanent or permanent filler, then it will require some form of intervention. Though there is a risk of not resolving the problem and a repeat treatment may be necessary, the more conservative/less invasive treatment is generally preferred.

Treatment

In some patients with minor complications such as bruising, observation and reassurance are appropriate. If action needs to be taken for a complication, this should be promptly performed. For lumpiness, mild asymmetry or mild overcorrection, gentle massage may be effective. In cases of significant asymmetry, a simple additional injection should achieve symmetry.

In the past for beading and small papules, spot dermabrasion or laser resurfacing has been advocated.²¹ While this intervention can be an appropriate measure, it would better to first initially attempt aspiration of the product—as long as it is not a permanent implant. Injecting the site with saline may increase the efficacy of aspiration. For granulomas secondary to superficial placement of hyaluronic acid, the injection of hyaluronidase should remove the offending agent with a minimum of trauma.²² Intralesional steroid injections also have been widely used for foreign body granulomas caused by implants.¹⁶ Although this treatment is effective, it should be used judiciously and in weak concentrations (no greater than 10 mg/mL) because it can result in adjacent skin atrophy and erythema. It may require multiple injections over time which can not only increase patient anxiety, but also the risk of an adverse effect. Some unapproved long-lasting implants have seen higher rates of infection which can be difficult to manage. In one case study, polyacrylamide gel resulted in a delayed infection in which antibiotics were ineffective, though intralesional steroids resolved the lesions.²³

In severe incidences of foreign body reaction, conservative measures are not effective, and surgery is the best option despite the subsequent scars.^{24,25} In the tear trough, slit excisions and teasing out the granulomas should be effective. However, in larger areas a formal ellipse may be necessary and/or a soft tissue flap may be necessary. While the recovery time can be extensive, if the rules of facial reconstruction are followed, the scars can be camouflaged.

Although large delayed granulomas are the most challenging of the long-term adverse effects to treat, the most feared early complication is necrosis due to inadvertent injection into a vessel and embolization (Fig. 5). Although necrosis may result from this complication, it is more likely—given the robust facial vasculature—that compression of several small blood vessels is the culprit. If blanching or duskiness does occur, then massage, nitropaste and possibly heparin



Figure 5 Partial forehead necrosis following a glabellar injection of hyaluronic acid gel. (Color version of figure is available online.)

injections may restore the local blood supply. Obviously, avoidance of overinjection would lessen the risk of this dreaded complication.

Summary

Volume restoration is an important aspect in facial rejuvenation. When used in indicated patients and with proper technique, implants can dramatically reverse facial aging. However, it is crucial to understand the limitations of each implant and the proper depth in which to inject them. Common complications include bruising, asymmetry and superficial papules. Delayed granulomas are more likely to occur in semipermanent fillers. Observation, additional filler, steroid injections, and surgical excision are customary methods to correct these adverse affects.

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