

Understanding How to Prevent and Treat Adverse Events of Fillers and Neuromodulators

Glynis Ablon, MD, FAAD

Summary: Experience teaches cosmetic surgeons to become good, but avoiding and treating adverse events make them great. In no area is this more true than in cosmetic procedures involving fillers and neuromodulators. By utilizing knowledge of materials and anatomy involved, specialists seek to avoid complications. A well-trained physician is able to reduce the sequelae from an adverse event by acting promptly using algorithms and a methodical approach to treatments. In this article I discuss the difference between perceived and true complications from fillers and neuromodulators, how to avoid, what to look for and how to treat to provide patients with the best possible outcomes, and make the physicians life less stressful. (*Plast Reconstr Surg Glob Open* 2016;4:e1154; doi: 10.1097/GOX.0000000000001154; Published online 14 December 2016.)

Experience teaches cosmetic surgeons to become good, but avoiding and treating adverse events make them great. In no area is this more true than in cosmetic procedures involving fillers and neuromodulators. By utilizing knowledge of the materials and anatomy involved, specialists seek to avoid complications. A well-trained physician is able to reduce the sequelae from an adverse event by acting promptly using algorithms and a methodical approach to treatments. In many instances, dealing with complications may be iterative because no 2 complications are exactly the same. However, by understanding the etiology and using an algorithm, it is possible to have a solid foundation.

When injecting fillers and toxins, it is imperative to differentiate between real and imagined complications. Each injection entails some degree of risk, and all of the potential complications should be in the informed consent signed by the patient. In addition, the most frequent and significant adverse events should be discussed before the procedure. Common treatment-related adverse events may be perceived by patients as complications if they do not expect to encounter them. For instance, bruising, pain, edema, erythema, needle marks, and asymmetry are all events that are common with any type of procedure

involving an injection. However, true complications are the ones we are primarily concerned about. These include scars, infections, granulomas, persistent lumps, droops and ptosis, visible palsy, and vascular occlusion. By understanding the anatomy and the materials being injected, it is possible to decrease the probability of a complication and to mitigate the outcome should one occur.

FILLERS

When injecting fillers, especially thicker ones, it is essential to understand the anatomy of the area being treated. Whether the injections involve the face, neck, chest, hands, or any other body part (we use fat currently to fill breast tissue as well), understanding where the nerves, arteries, and veins are is critical. Next, one must understand the properties of the filling agent being injected. Before injecting, a complete filler, trauma, and surgical history should be obtained. Any of these may increase the risk of complications and warrant a more conservative approach. As with any procedure, appropriate photographic documentation is essential, especially when managing imaginary complications.

From the Department of Dermatology, UCLA School of Medicine, Los Angeles, Calif.; and Ablon Skin Institute & Research Center, Manhattan Beach, Calif.

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To minimize the risk, this author begins each consultation with an information sheet that clearly defines the pre- and posttreatment instructions. This is an essential part of the consultation, and I document it as such. The lead author uses a consent that warns of every possible, perceived, or true complication, even blindness. Patients are warned to avoid nonsteroidal antiinflammatory medications, aspirin, vitamin C, and $\omega 3$ supplements. I suggest arnica tablets and bromelain (found in pineapple) to reduce bruising risks.^{1,2} It is recommended that patients sleep with the treated area elevated for 1 to 2 nights after injections. Ice water bags applied to treated areas for 5 to 10 minutes per hour will reduce swelling/edema and trauma. It is important to instruct patients to avoid leaving the ice on continuously for more than 10 to 15 minutes. Many of this author's patients choose to continue arnica, ice water bags, and elevation. When a bruise appears, it is useful to offer pulsed dye laser treatments to speed resolution.³ Applying Cytoactive may help to clear bruising via a theorized transport of glycerol through the layers of the skin, followed by hydration of the tissues by glycerol and water. This may displace blood and minimize bruising.

There are several ways to reduce the risk of adverse events while performing injections. First, it is well documented that there is a direct correlation between the speed of injections and the number of complications.⁴ Therefore, it is essential to decrease the speed of injections. This author typically spends 5 to 7 minutes per milliliter of filler. Using the smallest gauge needle also slows the administration of filler. I always apply a topical cooling device that reduces pain and bruising⁵ after applying topical anesthetic like Pliaglis, LMX-4, or compounded triple anesthetic agent for 20 minutes before starting procedures. One can choose to use cannulas for delivery of any filler. The use of a cannula will reduce bruising as tips are not sharp. Massage is helpful with many fillers, but not all, to reduce "lumps and bumps." If lumps or bumps cannot be massaged away after 7 to 10 days, it is possible to digest hyaluronic acid fillers with hyaluronidase. Alternatively, it is also possible to extrude many fillers by using a puncture with a 26-gauge needle or an 11 blade.⁶ Lumps caused by fat injections will sometimes respond to hyaluronidase or corticosteroid injections. Similar to the treatment of lumps and bumps, these same techniques may also be utilized for areas that have been overcorrected with a filler material.⁷ One adverse event that may be noted frequently is the swelling associated with injections of calcium hydroxylapatite into the dorsum of the hands. To minimize this swelling, I place 1 to 1½ cc split between both hands, knowing that I will likely need more, but the additional filler is placed at follow-up visit in 1 month. Subsequently, swelling has not been an issue.

Granulomas are more commonly seen with nonhyaluronic acid-based products such as silicone, poly-L-lactic acid, and polymethyl methacrylate. Each of these may form microspheres that can be extremely difficult to treat. Treatment with hyaluronidase, collagenase, and steroids has demonstrated to help these granulomas. In some instances of granulomas, surgical removal is the definitive treatment. When the granulomas undergo delayed in-

flammation, treatment with oral antibiotics and cyclooxygenase-2 inhibitors may help to minimize the swelling.⁸ When injecting the neck and chest, the use of the microdroplet distribution of hyaluronic acid-based products may help to decrease the risk of granulomas. Hyaluronidase is used at 20 to 60 units per 1-mL filler. Triamcinolone is injected to females (2.5 mg/mL) and males (5 mg/mL) with 0.1 mL per granuloma (0.2–0.6 cm; dosing is an experience-based value from this author and compilation of articles).⁹ For necrosis, the dosage is a minimum of 200 units¹⁰ of hyaluronidase.

Vascular compromise has been reported to occur in a large, retrospective study at a rate of 0.05%.¹¹ In addition to speed of injection, it is imperative to inject in the proper plane for the desired outcome. In addition, knowledge of where the nerves, arteries, and veins are will help to avoid the "danger zones." Filling of the temporal fossa should be done at the periosteal plane to avoid the superficial temporal artery. Injections into the forehead also need to be in the deep planes to avoid the superficial vessels that are abundant in the region.^{12,13} However, in the glabellar area, a high-risk danger zone, placement of any filler must be carefully and more superficially injected to avoid vascular occlusion and necrosis of the supraorbital and supratrochlear arteries.¹⁴ Other significant danger zones include the angular artery at the base of nasal labial fold and the superficial labial artery at the corner of the mouth. One other significant potential hazard is the dorsal nasal artery located at the root of nasal/glabellar groove,¹⁴ and similar care with slow injection technique, attention to anatomy, observation of patient pain or discomfort, and cannula use will reduce these risks.

More serious and true complications with fillers include vascular occlusion and necrosis.¹¹ As one injects any filler, it is critical to watch the surrounding tissue. Upon placement of the needle, aspirate to observe that there is not intravascular placement. If no flash of blood is seen, slowly inject filler and observe the surrounding skin for blanching, vascular flash, reticulated erythema, or a purple/dusky/grey-blue hue. Many authors also report that intense pain in the treatment area may be another sign of vascular compromise.¹⁵ If any of these situations occur, immediately stop the injection and flood the area with hyaluronidase. Recommended dosages vary, and there has not (to this author's knowledge) been a controlled trial comparing different doses. It is better to overcompensate with hyaluronidase than to undercompensate. Immediately after this, apply nitropaste (2%) and reapply this twice a day. Warm compresses and vigorous massage are also critical to improving the blood flow to the area. Patients should also be given baby aspirin immediately to inhibit platelet aggregation. By limiting the amount of product injected in a given injection and by applying minimal pressure on the syringe, it is possible to decrease the risk of retrograde flow into the retinal arteries. This type of low pressure/low volume injection also decreases the risk of vascular compression. If a patient has a suspected vascular compromise, it is best to keep them under observation for a period of at least an hour and usually more. This will enable additional treatment. The use of hyperbaric oxygen

is controversial, but in the event of a significant vascular compromise, its use should be considered. The immediate use of steroids is also recommended. Doses used range between 20 and 60 mg of prednisone, and this should be continued for several days to decrease the inflammatory component of the injury. Finally, the addition of erectile dysfunction drugs to dilate vessels should be considered, which is really anecdotal.

The most serious complications from soft-tissue augmentation include retinal artery occlusion and cerebral embolism. These have been observed primarily with injections of fat but have also been seen with hyaluronic acid products.¹⁶ Fortunately, these are extremely rare. However, the risk increases as the volume of injections and the number of injections increase. Decreased visual acuity, pain in the orbit, headache, nausea, dizziness, and ptosis may all signal a significant issue and should be attended immediately. Ophthalmologic consultation should be sought immediately if these symptoms are present. The presence of any of these symptoms warrants consideration of treatment with hyaluronidase, warm compresses, application of nitropaste, and aspirin. Loss of vision, when it occurs, is usually permanent.¹⁷ Collaboration with an ophthalmologist is crucial in these patients.¹⁸ Before treating the glabella, nasolabial crease, or tear troughs, it is essential to have a great deal of experience and anatomic knowledge to minimize the risk of vascular compromise.

NEUROMODULATORS

One of the most comforting features about adverse events with neuromodulators is that they are typically transient. Because the mechanism of action of the toxin involves a temporary blockage of the release of the neurotransmitter acetylcholine, its effects are also transient. These proteins are used to treat a range of conditions including hyperhidrosis, migraines, cervical dystonia, spasticity, as well as for their cosmetic indications. As such, there is a wealth of information regarding adverse events associated with their usage.¹⁹

In the cosmetic realm, the most common adverse events are injection related. These include bruising, swelling, edema, needle marks, pain, and bruising.¹⁹ In addition, toxin-related events such as ptosis, asymmetry, diplopia, and dysphagia are temporary in nature.

As with any injection, it is imperative to provide each patient with informed consent. In addition, pre- and post-treatment instructions are very important. Consent forms should be extensive, and refer to the information contained in the package insert. For patients who want to see the entire package insert, an opportunity to read it should be provided. One of the best ways to minimize the risk of an adverse event is to minimize the treatment. Injecting less neuromodulator than may be required, followed by a follow-up treatment, is a safe way to obtain more natural and less risky result. As with any cosmetic procedure, one critical means of minimizing the perception of an adverse event is to obtain photographs. This frequently serves to demonstrate to the patient not only the benefits of the treatments but also to show them that perceived “new”

lines and folds, as well as vascular structures and nevi, were present before the injections.

The most common complication associated with botulinum toxin injections in the glabella and frontalis is brow or lid ptosis. The brow ptosis typically occurs when the frontalis muscle is overtreated or when the levator palpebrae muscle is inadvertently injected. Negating the levator function of the frontalis can result in a brow that becomes ptotic. One method of minimizing this risk is to avoid treatment of the bottom 1/3 of the brow and, in some patients with brow and/or lid ptosis, avoid brow injections entirely. During the consultation, it is important to discuss the brow and obtain an understanding of the patient's desired shape. In general, females prefer an arched brow with the peak of the arch located at the lateral aspect of the iris. Males tend to prefer to have a flat brow that does not feminize their face. Perhaps the best method of avoiding complications with toxins in the upper 1/3 of the face is to use less toxin than may ultimately be needed and then to revisit the area in 10 to 14 days. Injections of toxins into the tail of the brow can help to lift the forehead and is an excellent way to avoid brow descent.

True lid ptosis occurs when the toxin is injected into the levator palpebrae superioris muscle. Fortunately, this is a complication that is rarely seen. It is believed that injections that are placed too inferiorly in the supratrochlear region can increase the risk of this occurrence. It has also been seen in a patient who went for a massage the next day after her toxin injections. Because of this risk, it is prudent to avoid massages for a few days after injections with toxins, so I recommend no massages for 1 week after these injections in my informed consent. Despite the fact that this is a temporary event, patients are uniformly irate when it occurs. The use of eye drops with naphazoline can help and are available without a prescription. More effective treatment may be obtained by using Apraclonidine 0.5% drops, which are available by prescription.²⁰ This solution is an α -2 adrenergic agonist that causes Müller muscles to contract and elevate the upper eyelid 1 to 3 mm. It is a quick fix, leaving patients happier until the effects of the toxin wear off. In skilled hands, 1/2 to 1 U of botulinum toxin placed in the medial and lateral tarsus can also lift a lid ptosis.

Another complication associated with toxin injections involves cheek paralysis or palsy. To avoid this, it is important to stay more superolateral with my injections around the crow's feet. Occasionally, I will place small amounts of toxin (4–8 U or onabotulinum toxin or 10–20 of abobotulinum toxin) in the upper cheek for lateral lines extending from the crow's feet. Higher doses here can lead to zygomatic minor muscle paralysis and result in a lip droop especially in older individuals. I add small aliquots to the intraorbital portion of the orbicularis muscle if it is hypertrophic. I warn patients that this may result in more open eyes that subsequently feel dry and may be difficult to close. To minimize the risk of dry eyes, it is critical to avoid infraorbital injections in patients with a history of transconjunctival blepharoplasties.

Advanced uses of botulinum toxin include treatments of the lower half of the face and neck. These areas are lad-

en with opportunities for adverse events. Because of this, it is important to achieve relaxation in a gradual manner rather than paralysis in an immediate one. Oral motor insufficiency may be seen with botulinum toxin injections around the orbicularis muscle. It is important to explain to patients when using toxins in this area that certain oral insufficiencies can occur. These may include difficulty drinking through a straw, whistling, playing the trumpet, and difficulty saying “P” and “B”s. An addition adverse event may arise when placement of the toxins is uneven. This may result in an uneven smile or drooling. To minimize this risk, it is worthwhile to use small doses of toxins and to avoid injections into the lateral 1/3 of the lip.

Even among expert injectors, treatment of the depressor anguli oris (DAO) may result in treatment of the depressor labii inferioris. This will result in a crooked mouth that is accentuated when smiling. This complication may be avoided by injecting small amounts of toxin and targeting the DAO in a gradual manner. Having patients move their mouth and palpating the DAO muscle help identify the correct placement of toxin. The only treatment for this type of complication is to intentionally treat the contralateral depressor labii inferioris to produce a symmetric mouth.

Injections of neuromodulators into the neck combined with injections into the mentalis muscle and DAO can lead to dramatic albeit temporary neck tightening and lifting. Injections of the platysma muscle can result in significant face lifting and relaxation of the bands that are one hallmark of an aging face. However, injections of toxin that are high dose or that are injected into the deep muscles of the neck may result in dysphagia. Treatment involves insertion of a feeding tube for those who are severely affected.

CONCLUSIONS

Patients expect cosmetic surgeons to enhance and enrich their physical appearance. Although it is vital to learn the advanced techniques necessary to do so, it is equally important to understand complications and adverse events that may arise. Although the best treatment for an adverse event is avoidance, it is imperative to know how to treat them when they occur.

Glynis Ablon, MD, FAAD

Ablon Skin Institute and Research Center
1600 Rosecrans Ave, Building 4B
Manhattan Beach, CA 90266
E-mail: drablon@abloninstitute.com

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