Managing AEs Associated with HA Fillers: An Update

Cosmetic dermatologists are becoming well-versed at handling adverse events, even when not their own. Here’s an update.

BY JOEL L. COHEN, MD

Outside of trials used to support FDA clearance of various hyaluronic acid (HA) fillers, reporting on adverse events (AEs) associated with these agents is inconsistent and unreliable. There are, therefore, limited data on rates of AEs associated with injections. However, the evidence we have suggests that rates are thankfully low.1 Risk for AEs can sometimes be related to injector skill, although even skilled injectors can see the development of AEs in their patients. The most serious potential AE associated with HA fillers is vascular compromise and subsequent risk of ischemia. There is a risk of visual compromise or even blindness if the filler material is carried to and blocks the retinal artery. Indeed, some cases of blindness caused by injection of fillers have been reported widely in the media.2 Injection into a vessel can lead to occlusion and account for almost all of these cases, while in extraordinarily rare cases an injection adjacent to a small vessel with a fixed structure behind it (such as bone) can create vascular compression.

The best defense against vascular compromise is avoidance. Great care should be taken when injecting in the most highly vascular zones of the face. Aspiration (pulling back on the plunger to assure that no blood is seen in the barrel of the needle) is one way to potentially help identify appropriate needle placement (i.e., outside of a vessel), although it is not fool-proof; it is very difficult to aspirate and then be in precisely the same exact spot to then inject product after repositioning from the aspiration. Similarly, use of blunt cannulas is thought to significantly reduce the risk of injecting into a vessel, but it is impossible to guarantee a cannula will not transect a vessel (smaller cannulas like 30g actually seem to be quite sharp).

Thankfully, vascular compromise can potentially be reversed. The key is to try to identify the problem as quickly as possible, and implement effective treatment. Back in 2015, I co-authored expert recommendations for the management of impending necrosis resulting from HA filler, and those guidelines continue to represent my current approach with trying to flood the area with hundreds of units of hyaluronidase enzyme.3 Recent consensus guidelines from the plastic surgery field echo our conclusions.4 The critical importance of this topic warrants a review of the recommendations.

MANAGING VASCULAR COMPROMISE

Every cosmetic dermatologist who performs HA filler injections should have hyaluronidase (marketed in the US as either Vitrase, purified ovine testicular hyaluronidase, or Hylenex, purified recombinant human hyaluronidase) on-hand in the clinic. Hyaluronidase degrades HA.

Our guidelines called for a minimum of 200U of Vitrase injected immediately at the first suggestion of impending necrosis. Larger volumes may be injected, depending on the area targeted and/or the amount of filler to be degraded. There is a very low incidence of hypersensitivity reactions to hyaluronidase, however, the risk of necrosis is sufficiently high that experts generally encourage initiation of treatment without a requisite skin test.

Hyaluronidase should be injected directly into the area where compromise is suspected (See table) and may be massaged to facilitate spread. Only a few injection sites are required for most cases. Injections may be repeated every one to two hours until evidence of very significant improvement or reversal is seen.5 4 Application of warm compresses (to increase vascular dilation and blood flow) and massage are also indicated at the first signs of impending necrosis.

Rates of adverse events tend to be low, and most AEs are reversible. The most significant potential AE is vascular compromise. Early identification and management of complications is essential to successful long-term management.

the bottom line
Most injectors are aware of the possible role for hyaluroni-
dase to reverse potential vascular compromise. Adjunctive
approaches may be less familiar. Diluting hyaluronidase with
lidocaine is thought to provide benefit in two ways. The
additional volume increases dispersion of the enzyme while
vasodilation from the anesthetic (without lidocaine) supports
needed blood flow. Alternatively, saline can be used to dilute
hyaluronidase, providing an increase in volume and subse-
quent dispersion but without additional vascular effects.

Awareness of the potential role for topical nitroglycerin
(NTG) paste has increased but warrants attention. Some
studies indicate that topical NTG instigates vasodilation and
thus could reduce the risk for necrosis.1 But, at least in one
animal study, there is controversy about nitropaste help-
ing treat necrosis. A recent paper related to a mental artery
occlusion after poly-l-lactic acid, found nitropaste along
with aspirin and warm compresses to be helpful.2 There is
a risk of orthostasis associated with application of topical
NTG, so patients should be in a prone position when it is
applied, (and the physician should apply with a glove).

Oral aspirin 650mg daily may be administered to theoreti-
cally prevent further clot formation due to vascular compro-
mise and is often continued for about a week.

A variety of additional interventions have been suggested
in addition to hyaluronidase +/- NTG paste +/- aspirin.
These interventions are aimed at healing the site of necrosis
(such as hyperbaric oxygen) or further supporting vascular
function. Our guidelines address these, and it may be worth
reviewing recommendations, keeping in mind that the criti-
cal role of intervention is to restore vascular function and
minimize or prevent any ischemic consequences.3

OTHER AEs

A more common but less serious AE associated with inject-
ble fillers is bruising. Risk of bruising always exists, but
the incidence may be technique dependent. Bruising is shown
to occur more frequently after injection into the dermal and
immediate subdermal planes and when using fanning and
threading techniques.4 Use of blunt cannulas has been pro-
posed to reduce the risk for also bruising, similar to necrosis.5

There is a lack of solid evidence for interventions to reduce
or prevent bruising. Patients who are prone to bruising may
temporarily withdraw aspirin or other known anticoagulant
therapies with the consent of the prescribing physician. I try
to avoid discontinuation of any “therapeutic anticoagulants”
as prescribed for a patient with a history of a heart attack, stroke,
blood clot, or AFib. If bruising is evident immediately post injec-
tion, pressure and cold compresses may help minimize it.

Both amica and topical vitamin K have been proposed
as antidotes to bruising. A randomized, placebo-controlled,
split-face study I conducted with Ashish Bhatia, MD found
that resolution of the field of purpura was consistently greater
with a vitamin K oxide gel after the second day of treatment.6
Differences in active versus placebo scores did not reach statisti-
cal significance during the nine-day study, however, there was
a trend toward faster resolution of purpura with active product.
Because topical vitamin K is safe and was not associated with
any adverse events, prophylactic application in the days prior to
injection may be recommended to interested patients. Pulsed
dye laser (PDL) has also been found to decrease bruising, and
is sometimes considered in the subsequent few days after the
filler session before the purple bruises turns yellow.

Less frequently addressed AEs related to injection of HA
fillers are hyperpigmentation and Tyndall effect. Patients
with darkest skin types may develop injection site post-
inflammatory hyperpigmentation (PIH).7 Any resultant
hyperpigmented macules thankfully tend to be small.
Treatment, if desired by the patient, is the same as for any
other incidence of PIH, including potentially topical reti-
noids, skin lighteners (either/or prescription or cosmeceuti-
cal grade), or topical azelacid acid. Bruising and hyperpigmen-
tation may also be addressed with energy-based devices.

When HA is placed too shallow, especially when particulate
HA fillers are inappropriately implanted into the superficial
dermis or epidermis, a Tyndall effect may be seen—leading to
a bluish appearance of the overlying skin. Hyaluronidase is the
treatment of choice, injected at the site of “bluing” to dissolve
the superficially-placed HA filler. Alternatively, a small gauge
needle or incisional technique may be employed to express
the improperly placed filler material.

Joel L. Cohen, MD, Director of AboutSkin Dermatology
(Greenwood Village and Lone Tree, CO), has published over
223 scientific articles and book chapters has co-authored
three textbooks. In 2018, he received the Melanoma Research
Foundation Humanitarian of the year Award.

References: