Commentary on: New High Dose Pulsed Hyaluronidase Protocol for Hyaluronic Acid Filler Vascular Adverse Events

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Soft tissue augmentation of the face has grown in popularity and demand in the past decade. Since the Food and Drug Administration approval of Restylane (Medicis, Scottsdale, AZ) in December, 2003, the number of approved hyaluronic acid fillers in the United States has increased, as has the public interest for these products.

As the incidence of injectable facial fillers has increased, so has the number of complications associated with vascular compromise from these injections. The need for early intervention with a treatment algorithm including hyaluronidase has been well established.

The article “New High Dose Pulsed Hyaluronidase Protocol for Hyaluronic Acid Filler Vascular Adverse Events” suggests a change in the treatment of patients with known or suspected vascular compromise after facial filler injection. Prior treatment protocols have included hyaluronidase, aspirin, topical nitroglycerin, warm compresses, and hyperbaric oxygen. The dosage and interval of hyaluronidase has been mostly anecdotal, and practitioners have usually injected this into the affected (compromised) area with usual follow up and reinjection in 24 to 48 hours. Because of the reported incidence of tissue necrosis and subsequent skin and soft tissue scarring, and the possible occurrence of blindness in the periorbital region, practitioners have increased their recognition and treatment of these problems.

This paper by DeLorenzi introduces a new treatment protocol for patients with vascular compromise secondary to occlusion from embolic events after facial filler injection. The paper suggests that only hyaluronidase is necessary to treat the occluded vessel(s), and that the treatment is best performed with an increased frequency than what has been suggested previously and by many clinicians. DeLorenzi terms the treatment high dose pulsed hyaluronidase. He recommends the repeated administration of high doses of injected hyaluronidase into the affected tissue hourly until resolution of symptoms and signs of ischemia. This includes that the tissue is no longer painful, regains normal color, and exhibits good capillary refill on physical examination. The protocol also proposes that other treatment modalities, such as aspirin, warm compresses, and topical nitroglycerin paste, are unnecessary and do not improve therapeutic outcomes.

DeLorenzi postulates that there are several reasons to suggest the need for more frequent hyaluronidase inject into patients with vascular compromise. These include the fact that after injection, the ischemic area produces a transudate that causes dilution and inactivity of hyaluronidase. Additionally, hyaluronidase begins to be degraded and diffuses away from the original injection site. DeLorenzi theorizes that these factors combine to reduce the action of the injected enzyme, thus necessitating repeat injection to produce the desired effect. He also notes that the same crosslinking that prevents the body from breaking down the product also serves to prevent more rapid degradation of the product when hyaluronidase is injected to treat a vascular obstruction.
The data to support the hypotheses in this paper are largely anecdotal. For example, the paper posits that vascular occlusion after filler injection is from embolic occlusion only, and does not occur from external compression of facial vessels. There is no scientific data or anatomic rationale to support this statement. In fact, it is probable that in regions where the skin is densely bound to the underlying tissue (such as the nasal tip) or in watershed vascular areas (such as the glabella), external vascular compression is more likely to be the cause of vascular compromise than is embolism. For this reason, vascular occlusion can occur without direct injection into the vessel lumen.

The pathophysiological mechanism requiring frequent repeated hyaluronidase injection is also not well supported by science. The reasoning for the reduced activity of hyaluronidase is not well documented. Because of this, the precise timing of the reinjection of hyaluronidase is not clear.

Even though the science behind DeLorenzi’s change in treatment for vascular occlusion is imperfect, his rationale is crystal clear and based on years of careful observation and modification of technique. The reasoning behind using multiple modalities of treatment (aspirin, hyperbaric oxygen, topical nitroglycerin, etc.) was clinical voodoo and certainly was not well studied. The astute clinical acumen of DeLorenzi recognizes one thing very well—that is, hyaluronidase works. His prior observation that larger doses of hyaluronidase are necessary to adequately treat impending vascular occlusion is now known fact that now benefits every filler injector. His present observation that patients with vascular necrosis require more frequent injection hyaluronidase than previously thought (every 1-2 days) is equally astute and based on his keen clinical observation. Additionally, his clinical observation that other modalities were adding very little to hyaluronidase in the “occlusion protocol” is also important. Simplifying treatment is always a positive strategy. Using multiple treatment modalities when complications occur obscures which treatment is actually effective.

This paper emphasizes the important steps in treating inadvertent vascular compromise after facial filler injection, namely that: (A) prevention of these problems including a thorough knowledge of anatomy, injection planes, and product is essential; (B) early recognition of the symptoms and signs are key and should be suspected; and (C) a treatment algorithm including frequent injection of hyaluronidase minimizes the chance that secondary negative effects of vascular occlusion, such as skin necrosis and scarring, occur. DeLorenzi has used his vast experience, keen observation, and clinical acumen to modify and improve existing the treatment algorithm.

The science will follow. Evidence-based medicine to specifically support this treatment formula will require carefully composed study. For now, this paper allows us to use careful observation and theoretical concepts of an astute physician to improve treatment protocols and lessen complication.

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