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Vascular occlusions can occur following dermal filler injection, leading to severe consequences for patients. Hyaluronidase, an enzyme introduced in general medicine in 1949, has gained widespread use in aesthetic medicine to dissolve hyaluronic acid (HA)-based fillers. This paper provides guidance on the indications and risks associated with using hyaluronidase for filler dissolution.Necessary steps are required to dissolve cross-linked hyaluronic acid (HA) in case of a vascular occlusion (VO). A VO resulting from an accidental intravascular injection is time-sensitive but not life-critical, unless visual or neurological disturbances occur. Failure to dissolve HA can lead to tissue necrosis, scarring, blindness, and/or cerebrovascular accident. Refer to the Complications in Medical Aesthetics Collaborative (CMAC) guideline for more information.The Tyndall effect is a phenomenon observed when particulate fillers are injected superficially, creating a blue hue due to the scattering of shorter wavelengths by filler particles. Historically attributed to light passing through particles with smaller wavelength than itself, this theory seems unlikely given HA molecules' larger size compared to light wavelength. Recent findings suggest that HA alters tissue physiology, allowing deeper absorption of red light, resulting in a blue appearance.Delayed-onset nodules can appear weeks or months after filler injection and are caused by various soft-tissue fillers, including cross-linked HA. Understanding the underlying pathophysiology is challenging due to limited access to investigations and patient reluctance for tissue sampling. Delayed hypersensitivity reactions, granulomas, and biofilms may contribute to delayed-onset nodules.Poor aesthetic outcome can result from incorrect filler placement, excess filler, or migration/redistribution. Good product knowledge, appreciation of three-dimensional anatomy, and correct technique are crucial for an optimal aesthetic outcome.As cross-linked hyaluronic acid breaks down in tissue, its physicochemical properties alter, affecting rheological parameters. Changes in these properties can affect the aesthetic outcome and contribute to dermal fillers migrating into areas of high muscle activity.In the UK, hyaluronidase is a prescription-only medicine licensed for enhancing permeation and uptake of subcutaneous or intramuscular injections, local anesthetics, and subcutaneous infusions. Its off-license use in aesthetic medicine to dissolve cross-linked hyaluronic acid must be disclosed as part of the consent process.Manufacturer's guidelines state the product should be stored at temperatures below 25C to maintain formula stability. It comes with an expiration date and can still be used until the last day of the month it expires if properly stored in temperatures under 25C. If stored above 25C, the expiration date will be affected. Once opened, the ampoule must be used right away and any leftover content discarded. If the clinician is outside the UK and has access to other hyaluronidase brands, they should follow the manufacturer's guidelines for storage instructions. Hyaluronidase can typically be reconstituted with common infusion fluids but is most commonly mixed with bacteriostatic sodium chloride (NaCl) 0.9% in medical aesthetics due to reduced pain upon injection. Both bacteriostatic and non-preserved NaCl have similar pH levels, which is crucial because enzyme activity is sensitive to pH changes. Bovine/ovine extracted hyaluronidase has a bimodal activity pattern with maximum activity at pH 4.5 and 7.5. However, in cases of vascular occlusions where pain might be due to ischemia, it's suggested that the patient should have hyaluronidase reconstituted with a local anesthetic without adrenaline to make the experience more comfortable. Hyaluronidase is physically compatible with lidocaine and often used alongside local anesthetics in eye or spinal anesthesia as part of blocks for administering anesthesia. It's recommended to always check manufacturer guidelines when verifying compatibilities with diluents, as formulations can differ by country. Concerns have been raised regarding the risk of a Type I hypersensitivity reaction when injecting hyaluronidase, prompting some clinicians to perform skin tests. However, according to the British Society of Allergy and Clinical Immunology (BSACI), these tests should be interpreted within clinical context, not used for screening drug allergies, especially in cases without symptoms pointing to an IgE-mediated allergy. Despite this, skin testing is commonly used in aesthetic medicine even when there's no reason to suspect allergy, which goes against BSACI recommendations. There have been rare reports of allergic reactions requiring adrenaline since 1949, with the incidence being extremely low unless large doses are administered intravenously, where the rate of Type I reactions increases significantly.When looking at reported cases of allergies, the overall incidence of allergic reactions is actually quite low (Table 1). Most allergic responses are localized and occur within an hour or later after injection, unless large doses are given intravenously. It's also important to note that incidence rates don't specify first exposure versus subsequent exposure, and allergies are mostly linked to prior exposure to hyaluronidase or bee/wasp venom.Studies have shown varying rates of allergy to hyaluronidase depending on the route of injection (Table 1). However, there are only a few documented cases of allergy after using hyaluronidase for aesthetic purposes. While some countries use compounded hyaluronidases with more impurities than ovine- or bovine-derived products, others like the US use recombinant hyaluronidase (Hylenex) which is considered to be the purest formulation.Some researchers believe that the problematic protein in hyaluronidase formulations is the enzyme itself. However, the presence of protein impurities within the formulation can also contribute to allergic responses. Thimerosal, a preservative used in some products, has been known to cause allergic reactions. Hyaluronidase produced by Wockhardt in the UK doesn't contain any excipients, but may still have impurities due to the manufacturing process.There haven't been any studies that isolated and tested protein impurities within all hyaluronidase products or established links between allergy and these impurities. Interestingly, there have been no documented cases of allergy with Hylenex, which is a human recombinant product.Hyaluronidase allergy cases have consistently shown enzyme as the direct cause of the allergic reaction, with some studies suggesting that route of administration and dosage may play a role in determining the severity of symptoms. In general, reactions are localized to the injection site, but higher doses or intravenous administration can lead to more generalized symptoms. Ocular administration is particularly common, likely due to longer residence times in ocular tissue, which may result in greater exposure to the drug. However, the accuracy of this proposed half-life has not been verified. Side effects from hyaluronidase, especially at concentrations above 1:10, can be irritant and include erythema and swelling, typically resolving within 24 hours. While these are predictable Type A adverse reactions, some patients with a history of allergy to other drugs or conditions may experience more severe responses.Allergic reactions to wasp/bee stings require careful consideration prior to administering hyaluronidase. A possible or confirmed allergy to bee and/or wasp stings poses a significant risk of cross-reactivity. Assessing the type of reactions and known information about allergy status is crucial. Small local reactions around the sting site are normal, whereas large localized reactions and anaphylactic reactions carry higher risks. Anaphylaxis risk increases if a patient has had a large localized reaction (LLR) or anaphylactic reaction to bees or wasps. Hyaluronidase contains multiple allergens, including hyaluronidase itself; without specialist testing, the clinician must assume this as the culprit. Administering hyaluronidase carries risks of up to 5% and 60% for LLR and anaphylaxis, respectively. For patients with a history of LLR or anaphylaxis, intradermal tests should be performed at an allergy clinic with full testing and support available. No validated concentration exists for assessing hyaluronidase allergy in the UK; case reports suggest 15-150 units/mL to verify allergy. The volume injected for an intradermal test is around 0.02-0.05mL, aiming for a 5-mm bleb.et al26 reported a need to concentrate hyaluronic acid (Restylane) from 1.5u/mL to 150u/mL for a positive IDT reaction, with lower concentrations resulting in negative outcomes. A study by Vartanian et al40 investigated local reactions using 10, 20, and 30 units of hyaluronidase to dissolve HA after injection into the arm. The authors found that higher doses led to more severe reactions.However, it is well known that hyaluronidase can cause local irritation when injected, as a predictable type A reaction. It remains unclear whether the reactions reported in Vartanian et al40 were allergic Type IV reactions or predictable irritation from injecting the drug. In patients with a history of anaphylaxis to bee and wasp stings, performing intradermal testing without validated test concentration can be hazardous.Reliable testing requires valid and sensitive results. Current skin test practice is neither valid nor reliable due to the lack of standardized test concentrations. Clinicians must consider this when interpreting IDT results. Performing an IDT involves careful steps outlined in Tables 2 and 3, with recommended dosages varying depending on the formulation.If performing an IDT, follow these steps: clean the area, stabilize the skin, inject a small amount of the drug, and use a control solution as a reference. The reaction can be positive if it results in a raised bleb surrounded by swelling and redness. In some cases, erythema may develop at the injection site.Given article text here The optimal dose and concentration of hyaluronidase for treating cross-linked HA in filler injections can vary depending on several factors, including the density of filler particles and tissue volume. While some studies have investigated the degradation rates of various fillers in response to hyaluronidase, more research is needed to determine the most effective treatment protocols.Literature suggests that using a higher dose of hyaluronidase may be more reliable than specific dosages, with clinicians treating "to effect" rather than adhering to established guidelines. However, previous studies have reported doses that are often conservative, and CMAC recommends using at least 1,500 units in 5mL for optimal treatment.Following elective treatment with hyaluronidase, patients can be reassessed after 48 hours, with additional treatment repeated as needed. However, it is essential to wait until swelling has subsided, typically taking two weeks or longer, to ensure a predictable aesthetic outcome.In the event of vascular occlusion, CMAC recommends following specific steps for management, including video recording, skin disinfection, and reconstituting hyaluronidase with bacteriostatic NaCl. Treatment should focus on achieving full coverage and treating "to effect," with reassessment of capillary refill time after each application.Additionally, CMAC proposes revising the frequency of administration of hyaluronidase based on pharmacokinetic modeling, which suggests that its systemic half-life is less relevant in aesthetic medicine.Following rodent studies, it has been documented that after subcutaneous and intramuscular administration of a particular substance, its half-life is approximately 5.1 minutes and 7.5 minutes, respectively.45 Hyaluronidase acts as a dispersal agent, effectively moving the injected diluent away from the injection site.6 Given the pharmacology of hyaluronidase and its brief half-life in both subcutaneous and muscular tissues, CMAC advises administering the initial dose with firm massage before reassessing vascular flow. If necessary, hyaluronidase should be readministered at this point if blood flow has not been established. Re-dosing is estimated to occur around 15 to 20 minutes after the initial dose following reassessment.CMAC also recommends co-administering hyaluronidase with lidocaine without adrenaline (or an equivalent local anesthetic agent) if available, as it results in a more tolerable experience for the patient and reduces patient fatigue. Additionally, lidocaine causes vasodilation in dermal tissues, which is advantageous in cases of ischemic injury.CMAC introduced the concept of stages of vascular occlusion in their guideline for managing hyaluronic acid filler-induced vascular occlusion. While this concept does not allow for assessing depth of ischemic insult, it provides some guidance on whether necrosis is present. CMAC agrees that supportive treatment and ancillary medicines are not required if ischemia is managed early; however, a patient presenting late with established necrosis will require wound management.Supportive care should be given to ensure no infection and optimal conditions for healing. The use of a hyperbaric chamber alone is not optimal for managing established necrosis.46 Table 5 outlines the proposed changes.The use of hyaluronidase in aesthetic treatments requires careful consideration of the depth and site of injection to achieve optimal results. When administering the enzyme, it's essential to focus on the area containing cross-linked HA, rather than treating the entire area, unless there's widespread swelling. The hyaluronidase will spread throughout the tissues after subcutaneous injection, and in cases of vascular occlusion or nodules, specific treatment protocols must be followed.The authors recommend that clinicians inject directly into nodules, taking note that resistance may occur during the process. However, it is crucial to attempt to penetrate the nodule to successfully remove the filler. Repeat treatments may be necessary, especially for larger issues, and patients should be informed of this possibility.Experience with ultrasound has shown that penetrating pockets of filler with a blunt cannula can be challenging without visualization, leading to incomplete resolution of the issue. In such cases, referring the patient for further imaging guidance or using ultrasound-guided dissolution may improve outcomes.This article discusses the use and potential risks associated with hyaluronidase in ophthalmology. A review of various studies and articles reveals that hyaluronidase can cause allergic reactions, including angioedema, anaphylaxis, and other immune responses.The article highlights several case studies and research papers that investigate the effects of hyaluronidase on skin and tissue permeability. For example, a 1979 study found that hyaluronidase preparations may contain contaminants that affect their efficacy.Other studies have explored the use of hyaluronic acid and its breakdown products, such as hyaluronidase, in cosmetic and medical applications. Researchers have investigated the properties of hyaluronic acid and its interactions with other substances, including sodium chloride.The article also mentions several clinical guidelines and protocols related to drug allergies, including anaphylaxis and other allergic reactions. These guidelines provide recommendations for identifying and managing potential allergies to hyaluronidase and other medications.Overall, the text suggests that while hyaluronidase is a useful tool in ophthalmology, it can also pose risks of allergic reaction and other adverse effects. Therefore, it is essential to carefully evaluate its use and monitor patients for potential side effects.Note: I condensed the original text into a shorter form, highlighting key points and concepts, while maintaining the overall structure and content.Several studies have documented cases of allergic reactions to hyaluronidase, a common medication used in various medical procedures, including cataract surgery and pain management. The symptoms of these reactions can be severe and include orbital inflammation, periorbital edema, raised intraocular pressure, and even anaphylaxis.In some cases, the reaction has been mistaken for orbital cellulitis or another condition. Delayed hypersensitivity to hyaluronidase has also been reported, occurring hours or days after exposure.The studies cited suggest that allergic reactions to hyaluronidase are rare but can occur in individuals with a history of allergies or sensitivity to other substances. In some cases, cross-reactivity to other allergens may be involved.Treatment for these reactions typically involves corticosteroids and antihistamines, although in severe cases, hospitalization may be necessary.Overall, the literature suggests that hyaluronidase allergy is a significant concern, particularly for individuals who receive this medication as part of their medical treatment.Hyaluronic acid (HA) injections are widely used in various medical and aesthetic procedures, including cataract surgery. However, some patients may experience adverse reactions to HA, such as anaphylactic shock or allergic contact dermatitis. Research has been conducted on the role of hyaluronidase, a naturally occurring enzyme that breaks down HA, in plastic surgery, cosmetic dermatology, and cancer chemotherapy. Studies have shown that hyaluronidase can enhance the absorption of HA fillers, reduce inflammation, and improve the efficacy of HA injections.However, some patients may be at risk of developing hypersensitivity reactions to hyaluronidase, which can lead to serious complications such as anaphylactic shock. Researchers are exploring new protocols for using high-dose pulsed hyaluronidase in conjunction with HA fillers to minimize the risk of vascular occlusions.Additionally, guidelines have been established for managing HA-induced vascular occlusion and optimizing the use of hyaluronidase in cosmetic dermatology. A literature review has also highlighted the potential benefits and risks associated with using hyaluronidase in various medical procedures.Overall, while hyaluronidase is widely used in medical and aesthetic applications, its effects can vary from person to person, and further research is needed to fully understand its role and optimal use in these contexts.Articles from The Journal of Clinical and Aesthetic Dermatology are made available here thanks to Matrix Medical Communications, as shown in Figure 1. This figure features common bees and wasps within the Hymenoptera order, adapted from Bonadonna P, Scaffidi...