**An Overview of Complications and Treatment Strategies in Periocular Dermal Fillers: A Literature Review**

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**ABSTRACT**

**Introduction:** The dermal filler market is a continuously expanding billion-dollar industry with the number of performed injections growing concurrently with the amount of post-injection complications**.** Most adverse events are mild and resolve spontaneously. Ischemic complications due to accidental intra-arterial filler injection may lead to skin necrosis and even irreversible vision loss.

**Aim of the study:** This review aims to critically evaluate the use of dermal fillers in the periocular area, possible post-injection complications and treatment options for adverse events, providing further guidance for aesthetic medicine doctors.

**Methods:** Databases such as PubMed, Medline and Research Gate were searched for articles published over the last 20 years.

**Results:** Dermal fillers in the periocular area are often chosen over surgical procedures due to their efficacy and outstanding safety profiles.

The reversing agent hyaluronidase causes hyaluronic acid fillers to be the primary choice for periocular filler injections. Post-injection complications after permanent fillers may require surgical excision.

**Conclusions:** The periocular region is exceptionally demanding, requiring excellent anatomical awareness and proper administration techniques for uneventful procedures. Individually adjusted treatment plans and proper product selection is crucial. Doctors must follow preventative guidelines to minimize the complication risk, including aspirating before injecting the product, performing injections in the mid or deep dermal plane and administering small volumes with slow injections. Imaging techniques are significantly beneficial for minimizing the risk of the most severe ischemic complications.

**Keywords:** dermal fillers, periocular, hyaluronic acid, calcium hydroxylapatite, poly-lactic acid, polymethyl methacrylate, polyalkylimide, hyaluronidase, complications, vision loss, treatment

**INTRODUCTION**

The periocular region, which encompasses the tissues surrounding the orbit, is among the earliest anatomical sites to exhibit visible manifestations of facial aging. Rejuvenation of this area aims to restore a more youthful and refreshed appearance by addressing dermal thickness, apparent soft tissue laxity, redundancy of upper eyelid skin, pseudoherniation of orbital fat and tear - through deformities [1].

Non - surgical procedures involving the use of dermal fillers are increasingly favored due to their effectiveness and accelerated recovery compared to surgical interventions, with over 3.4 million injections performed in the United States in 2023 [2]. The dermal filler market was valued at $6.3 billion globally in 2023, and by 2033 it is projected to reach $16.8 billion [3]. The most widely used dermal filler for rejuvenation of the periorbital region are hyaluronic acid gels (HAGs), which were first FDA - approved in 2003 (Restylane; Galderma) [4]. Hyaluronic acid is a polysaccharide polymer, a natural component of the human dermis, which acts as a matrix for collagen production [5]. Due to its hydrophilic properties, it can retain water, and therefore, volumize and hydrate the overlying skin [6]. Other commonly administered fillers include calcium hydroxylapatite, poly-L-lactic acid, polymethyl methacrylate and polyalkylimide [7].

Those products are characterized by a remarkable safety profile, however, the periocular area with numerous delicate anatomical structures poses great challenges even to the most skilled injectors. The spectrum of possible complications is broad with the vast majority being temporary, mild adverse events that resolve spontaneously or can be reversed with a hyaluronidase injection. Those can include bruising and swelling, displacement or migration of the filler, contour irregularities, Tyndall effect, malar edema, or granuloma formation. Nevertheless, severe ischemic complications have been reported with an incidence of 0.003%, due to accidental intra - arterial injection that may lead to skin necrosis and even irreversible vision loss [1,8,9].

Certain precautionary steps can be taken to minimize the possibility of complications. An in - depth review of patient’s medical history, previous adverse events or anaphylactic reactions, appropriate selection of products and procedures can all prepare medical professionals to provide the highest level of care and an individual approach to every patient [1].

This review aims to critically evaluate current literature on the injection of dermal fillers in the periocular region. It will assess the most commonly used fillers, possible complications of their application, preventative methods and treatment options for adverse events, providing guidance for healthcare providers on how to effectively address these challenges.

**METHODS**

A literature review was conducted by a thorough search of databases such as PubMed, Medline, and Research Gate using keywords: “dermal fillers”, “periocular”, “hyaluronic acid”, “calcium hydroxylapatite”, “poly-lactic acid”, “polymethyl methacrylate”, “polyalkylimide”, “hyaluronidase”, “complications”, “vision loss”, and “treatment”. The articles published over the last 20 years were analyzed to provide an in-depth evaluation of periocular dermal fillers, post-injection complications reported during this time and the proposed treatment options.

**DERMAL FILLERS**

***Hyaluronic acid filler***

Hyaluronic acid (HA) is a linear polysaccharide naturally occurring in soft connective tissues. It is formed from disaccharide units of N-acetyl-D-glucosamine and glucuronic acid. HA plays a key role in wound repair and tissue regeneration, acting as a matrix for collagen production.Synthetic HA fillers are often of bacterial origin, hence ensuring minimal protein contamination. Crosslinking after synthesis, commonly achieved by using 1,4-butanediol diglycidyl ether (BDDE), increases the product’s stability, since a natural HA has only a half-life of 12-24 hours [5,8,10]. Commercial fillers differ in their physical and chemical properties, including size of particles, concentration, indications, or sites of placement. HA fillers are temporary and biodegradable, lasting for 6 to 18 months, depending on the product and patient-specific factors, such as the expression of degradative enzymes. However, facial ultrasounds have shown the possibility of prolonged HA filler’s presence in patients’ tissues up to 36 months [7,8,11]. In case of unsatisfactory results or post-injection complications, hyaluronidase, an enzyme that degrades hyaluronic acid, is commonly used to dissolve the filler, hence reversing the procedure [12]. In addition to facial rejuvenation, they are used to improve the proportions and asymmetries of the face, therefore restoring balance and facial harmony by providing immediate hydration and volume to the skin, which may be used in the treatment of tear trough deformities [1,5,6]. Popular brands of hyaluronic acid filler include Restylane®, Juvederm®, Perlane® and Belotero® [11,13].

***Calcium hydroxylapatite***

Calcium hydroxylapatite(CaHA) is a biodegradable and biostimulatory dermal filler, second most popular in the periocular area [7,14]. The CaHA dermal filler consists of 30% of synthetically produced uniform calcium hydroxylapatite microspheres suspended in 70% of sodium carboxymethylcellulose (CMC) gel carrier [13,15]. The constituent of these microspheres is a synthetic form of a mineral naturally present in teeth and bones [14]. These fillers are biosynthetically produced without the use of any animal-derived product, therefore minimizing the chance for an adverse allergic reaction in patients [16]. In 2003 it received Conformité Européenne (CE) certification and later, in 2006, Radiesse® became the only FDA-approved CaHA filler.

It is used for treating moderate to deep facial wrinkles and folds, and furthermore, as a treatment method in patients infected with the HIV virus suffering from facial fat loss [14,16,17]. Once injected, the CMC gel carrier is disintegrated while the CaHA microspheres stimulate collagen production. Hence, calcium hydroxylapatite can be referred to as a biostimulatory filler as it is gradually replaced by neocollagen. This process begins as early as 4 weeks post-injection [14]. The volumizing effect of the CaHA filler lasts between 12 to 18 months [17]. Due to the presence of calcium in CaHA fillers, the microspheres appear white underneath the skin, giving a light reflection and providing an immediate brightening effect, which can be a major advantage for patients with hyperpigmentation in the periocular area or visible venous circulation [18]. As opposed to HA fillers, in case of unsatisfactory results or post-injection complications, the effects of calcium hydroxylapatite fillers cannot be reversed. They may be treated by injecting saline to dilute it, allowing the aesthetic doctor to mechanically redistribute it with massage. More severe cases, e.g., painful nodules, may require intralesional steroid injections or even surgical excision [19].

***Poly-L-lactic acid***

Polylactic acid was first synthesized in 1954 from the α-hydroxy-acid family and has been used as a material for absorbable sutures, screws or resorbable plates in surgeries. Microspheres of its levo isomeric form, poly-L-lactic acid, in the powder form are the main component of Sculptra®, which is the only FDA-approved poly-L-lactic acid filler (PLLA) [13,20]. It can be characterized as a biodegradable and biostimulatory dermal filler, correcting the periocular loss of cutaneous volume by promoting the production of collagen by fibroblasts starting approximately 6 weeks post - injection [13,21]. Depending on the injection site, the results may remain for up to 2 years [11]. Sculptra® was first approved to treat HIV-positive patients with facial lipoatrophy, and in 2009, obtained approval for the treatment of deep facial wrinkles and nasolabial folds. To achieve desirable results a series of treatments with a few - week intervals may be needed. As this procedure does not provide instantaneous effects, it is often used in conjunction with hyaluronic acid or calcium hydroxylapatite fillers [13,16]. Once the PLLA fillers are injected, the results are irreversible, hence a proper choice of the aesthetic medicine doctor is crucial for these procedures [16]. Luckily, most adverse effects are mild and resolve spontaneously, most of them being nodules formed due to a too superficial placement of the product [13]. If necessary, intralesional corticosteroid injections or surgical excision may be performed [19].

***Polymethyl Methacrylate***

Polymethyl methacrylate (PMMA) is a nonbiodegradable, synthetic polymer, which is a component of artificial intraocular lenses and bone cement. The only PMMA filler authorized by the FDA is Bellafill®, composed of PMMA microspheres suspended in a solution of bovine collagen [11,16]. It can be administered to treat deep wrinkles, volume loss or to fill sunken scars. PMMA filler is considered to be permanent, lasting for approximately 5 years [22]. To achieve satisfactory results more than one session is usually required, due to the degradation of bovine collagen 4 to 6 weeks post - injection and it being only partially substituted with patient’s own collagen [23]. Injecting Bellafill® into deeper tissues or at the dermal-subcutaneous junction is recommended.

More superficial placement (intradermal) may result in permanent alterations to the color or texture of the skin, causing nodule or granuloma formation that can require intralesional steroid injections or surgical excision [24,25]. Bellafill® has been found to be a great long-term solution for patients with dark circles and tear trough deformities [25].

***Polyalkylimide***

Polyalkylimide is a hydrogel polymer and a derivative of acrylic acid [26]. It is a permanent, biocompatible soft issue filler used to treat nasolabial folds, deep wrinkles, depressed scars, or facial lipoatrophy in HIV-positive patients [27]. Due to its stability and hydrophilic properties it is applied in augmentations (e.g., gluteal, breast) as large volumes can be achieved by a single procedure.

The dermal filler Bio-Alcamid® is composed of 4% polyalkylimide gel and 96% water. Polyalkylimide fillers are not yet FDA - approved, however, they have been administered in Europe since 2001 [26].They imitate the adipose tissue in order to be encapsulated in the host’s collagen tissue, therefore becoming hydrolysis resistant in approximately a month post-injection [28]. Most complications include migration of the filler and formation of abscesses, which can be treated by puncturing the capsule and mechanically evacuating the filler or by a surgical excision combined with beta-lactam antibiotics for 14 days to treat the cutaneous infection [26,29].

Table 1 summarizes the key similarities and differences between the reviewed dermal fillers.

**Table 1.** Comparison of dermal fillers[7,11,12,13, 16,17, 21, 26, 30]

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Filler (manufacturer) | Temporary/  permanent | Reversibility | Composition | Durability | Biodegradability |
| Hyaluronic acid | Restylane® (Galderma) | temporary | Possible with the use of hyaluronidase | 20 mg/mL hyaluronic acid; particle size of 400 µm | 6-18 months | yes |
| Perlane® (Galderma) | 20 mg/mL hyaluronic acid; particle size of 750–1,000 µm |
| Juvéderm XC® (Allergan) | 24 mg/mL and 0.3% lidocaine |
| Juvéderm Voluma® (Allergan) | 20 mg/mL and 0.3% lidocaine |
| Belotero® (Merz Aesthetics) | 22.5 mg/mL hyaluronic acid |
| Calcium hydroxylapatite | Radiesse® (Merz Aesthetics) | temporary | Impossible | 30% calcium hydroxylapatite microspheres and 70% sodium carboxymethylcellulose carrier gel | 12-18 months | yes |
| Poly-L-lactic acid | Sculptra® (Galderma) | temporary | Impossible | powder of poly-L-lactic acid microspheres | 2 years | yes |
| Polymethyl Methacrylate | Bellafill® (Suneva Medical) | Permanent | Impossible | 20% polymethylmethacrylate suspended in 80% solution of 3.5% bovine collagen and 0.3% lidocaine | 5 years | no |
| Polyalkylimide | Bio-Alcamid® (Polymekon Research) | Permanent | Impossible | 4% polyalkylimide gel and 96% water | 5 years | no |

**COMPLICATIONS**

Despite an outstanding safety profile, adverse effects may occur due to dermal filler injections. Hence, the need for comprehensive knowledge among clinicians about the products, correct injection techniques and proper treatment of the arising complications [31]. These are dependent on the type of filler used and its application site. Temporary fillers usually lead to immediate complications, easily treated or resolved spontaneously, while permanent fillers can result in complex issues years after injections. Dermal filler complications can be classified based on onset time as immediate (up to 24 h post-injection), early (24 h to 4 weeks after the procedure) or delayed (over 4 weeks post injection) [19]. They may be also divided according to their severity into mild or severe and classified based on their mechanism into ischemic and non - ischemic [32]. Luckily, most adverse events of the periocular dermal filler injections are mild and transient, including bruising, edema, pain or redness of the injection site [7]. More complex and long-lasting complications may occur as nodule or granuloma formation, infections, Herpes reactivation, malar edema, filler migration, skin discoloration or Tyndall

effect, leading to the most severe ischemic adverse events like skin necrosis and visual loss [7,31].

Table 2 provides an overview of possible adverse effects after dermal filler injections classified based on their onset time.

**Table 2.** Overview of dermal filler complications [19,26,31,32 ,33]

|  |  |  |
| --- | --- | --- |
| Classification of complications | Onset time | Clinical presentation |
| Immediate/ Early-onset | During injection to 4 weeks after the procedure | * Ecchymosis * Erythema * Edema * Pain * Immediate hypersensitivity reactions * Nerve damage * Haematoma * Nodule * Infection * Herpes reactivation * Skin necrosis * Vission loss |
| Late- onset | over 4 weeks post injection | * Delayed hypersensitivity reactions * Tyndall effect/ blue-gray dyschromia * Hyperpigmentation * Filler migration * Malar edema * Nodule * Granuloma * Infection * Abscess |

**NON-ISCHEMIC COMPLICATIONS**

***Ecchymosis, erythema, edema***

Post-procedure ecchymosis, erythema or swelling are commonly occurring complications after all dermal fillers, usually resolving spontaneously, often evident after periocular filler injections because of the thin skin in this area. Slow injections with small filler volumes administered at the adequate level substantially reduce the complication rate [32].If possible, substances with an anticoagulant effect, such as non-steroidal anti-inflammatory drugs (NSAID), gingko supplements and anti – platelet - aggregating drugs should be discontinued approximately a week before filler injections. Moreover, studies have shown that administering the filler into immediate subdermal or dermal planes by incorporating threading and fanning techniques cause bruising more frequently [33]. Applying cold compresses, vitamin K creams or arnica prior and post injections, as well as, avoiding excessive exercise after the procedure can minimize the risk of erythema and significant bruising. In case of persistent erythema, topical steroids should be applied [32]. Depending on the severity, edema can be treated with cold compresses, non-steroidal anti - inflammatory drugs and anti-inflammatory enzymes (Wobenzym Vital or Bromelain) or steroids in severe cases [19].

***Immediate hypersensitivity reactions***

Immediate hypersensitivity reactions (Type 1) after dermal filler injections occur due to histamine being released in response to exposure to antigens [35].Within minutes of the injection, increased vascular permeability due to histamine release, causes localised or generalised erythema, edema, pain, itching and discomfort. Patients should be monitored due to the possibility of airway obstruction. The intensity of the reaction determines the course of treatment. In most cases the reactions are mild and do not require medication as they resolve spontaneously in a matter of hours or days. Antihistamines administered orally can reduce edema, however, persistent angioedema may be treated with oral corticosteroids [32,35].

***Delayed hypersensitivity reactions***

Delayed type hypersensitivity reactions (Type 4) may occur 1-3 days after injections. They are mediated by T cells activated as a response to antigens [35]. Possible symptoms can include edema, erythema, granulomas and induration. Treatment of persistent cases is based on administration of oral steroids and dissolving fillers with hyaluronidase or surgical excision [32,35].

***Nerve damage***

Nerve damage is a rather rare adverse effect of dermal filler injections that can be a result of the nerve’s partial or full transection by a needle or due to tissue compression [32,36]. Hence, temporary or permanent paresthesia, dysesthesia or anesthesia can occur [26].The most frequently injured nerve is the infraorbital nerve, situated about 7 mm below the inferior orbital rim at the mid-pupillary line, which affects sensation from the lower eyelid, cheek, lateral part of the nose, upper lip and upper teeth [33,37]. In rare cases, the facial nerve may also be affected, resulting in lagophthalmos and the exposure of the ocular surface [33].Treatment recommendations include steroid injections (triamcinolone), hyaluronidase injections, especially for HA fillers, or diluting the product with saline and cold compresses for reducing the edema [36].

***Tyndall effect/ blue-gray dyschromia***

A technique-dependent adverse effect associated with dermal fillers is the Tyndall effect [19]. When traveling through microscopic particles, blue light is scattered more than longer wavelengths. Therefore, a faint blue-gray discoloration appears where the filler injection was administered. This is caused by the filler being injected too superficially, especially in high-risk areas such as the tear troughs or superficial fine lines in the periorbital area [8,35].Treatment options include hyaluronidase injections to dissolve the filler, nicking the skin and mechanically evacuating the filler or performing a surgical excision [33].

***Hyperpigmentation***

Hyperpigmentation is especially common in patients with Fitzpatrick skin types IV–VI, however, it can be observed in all skin types [33]. The first line of treatment should include bleaching substances such as Retin-A (tretinoin) and topical hydroquinone (2–8%) along with high UV protection sunscreens applied daily. In more severe cases of skin discoloration chemical peels or fractional CO2 lasers may be applied [19,33].

***Malar edema***

Malar edema following periocular dermal filler injections, especially to treat tear troughs and infraorbital hollows, is a serious complication experienced by over 11% of patients [32,33].The superficial orbicularis oculi fat is divided into superficial and deep compartments by the malar septum. The lymphatic drainage of the superficial compartment is compromised, while for the deep compartment it is continuous with the cheek. Therefore, an excessive amount of volume or a viscous substance applied too superficially may compress the lymphatics, impairing drainage and leading to edema [35,37].

Malar edema may be chronic and challenging to treat. Head elevation, applying cold compresses, manual lymphatic massage and drainage, and intralesional corticosteroid injections (triamcinolone) are among the treatment recommendations [33,38]. In case of hyaluronic acid fillers, hyaluronidase injections should be administered [33]. However, the most effective preventative method is to match the procedures and fillers individually to every patient, apply limited volumes of filler in a single session and administer the product at the immediate preperiosteal level in the malar septum [32,35].

***Nodules***

Nodules are among the most frequent adverse effects of dermal filler injections. They can be described as a localized firm swelling or a lump [19]. In general, nodules can be classified as either non-inflammatory or inflammatory. Non - inflammatory palpable nodules result from incorrect and asymmetric filler placement or injections performed too superficially, whereas inflammatory ones are due to infection or an inflammatory reaction to the injected foreign body [36]. Nodules appearing after hyaluronic acid filler injections have a transient nature and if necessary, can be managed with hyaluronidase [19]. CaHA and PLLA are also temporary fillers, in which case nodules usually dissipate over time (2 - 6 weeks), however, if needed treatment with saline injections and redistribution of the product with massage is possible [1,19]. More severe and cosmetically unpleasing cases may require intralesional steroid injections or surgical excision. Poly-l-lactic acid filler nodules also bear a greater likelihood of being fibrotic, which may be treated with 5-fluorouracil. It allows the scar tissue around the implant to soften and the nodule to become less apparent [1]. Nodules after permanent dermal filler injections should be surgically removed using dermabrasion, punch excision, and micro-electric dissection [19].

***Granulomas***

Granulomas may form as a result of chronic inflammation, which is the immune’s system response to an injected foreign body that macrophages are unable to phagocytose [33,36]. They are considered a late-onset complication, forming months or even years after injection. However, granuloma incidence is rare, oscillating around 0.01 to 1%, even though they can occur after injections of all dermal filler materials [33]. A number of variables can increase the chance of granuloma formation including volume of the injected filler, superficial placement, intramuscular injection, small particle size, hydrophobic properties of the filler or prior occurrence of post-injection infections [36]. Granulomas can be treated with intralesional steroids, 5-fluorouracil, as well as, immunomodulatory and anti-inflammatory drugs, such as hydroxychloroquine, minocycline or rifampicin.

Intralesional injection with a combination of 5-fluorouracil and triamcinolone has been found effective in treating granulomas. Using tacrolimus, antihistamines or NSAIDs is an alternate choice [19,36].However, the most effective technique seems to be the removal of the dermal filler, which includes the use of hyaluronidase, especially for HA fillers. In case of poly-L-lactic acid, polymethyl methacrylate or polyalkylimide fillers, which lack a reversing agent, surgical excision is performed [7].

***Infections***

As dermal filler injections involve interrupting the skin’s continuity, they carry a risk of infections. Common skin pathogens like *Streptococcus pyogenes* or *Staphylococcus aureus* are typically the cause of acute infections, which manifest as abscesses or acute inflammation with edema and erythema at the injection site [32,33]. Since face cellulitis can lead to sepsis in susceptible patients, infections should be treated immediately after detection. If left untreated, preseptal cellulitis in the periocular area can develop into orbital cellulitis and cause visual loss. Mild infections can be successfully treated with oral antibiotics, whereas more severe infections may require antibiotics administered intravenously and patient’s hospitalization [32].The recommended treatment involves Flucloxacillin for 7 days, Amoxicillin with clavulanic acid for 10-15 days or Ciprofloxacin for 2 to 4 weeks [33]. If the involvement of the periocular area is present, an ophthalmological consultation should be performed. Surgical drainage may be required for abscesses that do not respond sufficiently to antibiotics. In order to prevent infections, procedures should not be performed on inflamed skin and the number of injections should be minimal with the avoidance of previous filler sites [32].

***Herpes reactivation***

Injections of dermal fillers may cause herpes simplex virus infections (HSV) to reactivate. Most herpes recurrences are observed in the perioral region, nasal mucosa, and the mucosa of the hard palate. Prior to injections, proper antiherpes prophylaxis should be prescribed to patients with over 3 episodes of severe cold sores [33,36]. The use of Valaciclovir 1g one day before and three days following the procedure is recommended. In case of active herpes lesions, patients should be advised to postpone filler injections until full recovery [33].

**ISCHEMIC COMPLICATIONS**

***Skin necrosis***

Vascular occlusion is rare, yet the most severe and feared adverse event occurring post dermal filler injections. The incidence of these complications is estimated to be 0.003% [37]. The most frequent cause is intravascular injection of filler into veins or arteries supplying the skin or mucosa, however, pressure from filler deposition or localized edema can also lead to vessel occlusion [32,33].Typical symptoms presented by patients include blanching and severe pain disproportionate to the injection, followed by livedo reticularis as a result of vascular obstruction. This causes swelling of the vessels, delayed capillary refill and a dusky, purple discoloration [35,39]. However, in some cases pain can be completely absent, hence causing diagnostic challenges for clinicians [40].

Late symptoms may include tissue necrosis and sloughing or blisters. The onset time depends on the mechanism behind the vascular occlusion with arterial embolic obstructions causing immediate ischemic symptoms, whereas venous compressions can take hours before becoming clinically apparent [35]. Moreover, a recent study revealed that 62% out of 52 surveyed injectors had unintentionally administered one or more intravascular injections in their medical career [40]. Treatment recommendations include an immediate stop of the injection and an aspiration attempt of the injected product, along with applying a warm compress and massaging the area.

Hyaluronidase ought to be administered immediately to the injection site and throughout the entire ischemic area, followed by a massage for better results, regardless of the type of filler as it reduces edema [33,39].Repeatedly performed injections may be required to treat the vascular occlusion. Acetylsalicylic acid, low molecular weight heparin, systemic or topical steroids and hyperbaric oxygen can also be administered as adjuvant treatment [32,33]. Phosphodiesterase type-5 inhibitors (e.g., sildenafil, tadalafil) can also improve the situation by dilating blood vessels, hence increasing blood flow to the ischemic area. Topical vasodilators, on the other hand, like 1or 2% nitroglycerin paste are no longer recommended, as they failed to indicate their beneficiary role in the recent studies performed on animal models.Dead cells and tissue constitute necrosis, which is susceptible to secondary infections, hence topical or oral antibiotics may be necessary to encourage healing and avoid further complications [40]. Finally, surgical debridement and wound closure are necessary for tissue necrosis, and skin grafts or rotating flaps may be required [33].

***Vision loss***

Although rare, vision loss due to dermal filler injections is the most devastating complication. In the 1980s, first cases of post aesthetic filler injections blindness were reported [41].Incidence rate of post-injection vision loss is greater for fillers administrated in the glabella, forehead, nasolabial folds and nasal region due to the challenging anatomy of these areas [33,39].An unintentional injection of the filler intravascularly causes the arterioles to expand, and the retrograde flow of filler emboli can occlude the ophthalmic artery or its branches, including the supraorbital, dorsal nasal, supratrochlear or central retinal artery, resulting in a loss of vision. Furthermore, it can cause periorbital pain, ischemic optic neuropathy, ischemia of the choroid, ophthalmoplegia, ptosis and even lead to cerebral infarction.Possible symptoms that should be associated with the possibility of occlusion of the ophthalmic artery or its branches include ocular pain, visual field defect, headaches, vomiting, nausea or other neurological symptoms [32,35]. Studies have shown that the recovery of palpebral position and ocular motility is possible, whereas visual loss is often permanent [42].

Treatment should include stopping the injection instantly, placing the patient in a supine position to lower the intraocular pressure and urgently transferring them to an ophthalmology department for assessment and further care [33,35].In order to avoid irreversible retinal ischemia, treatment should begin within 1 hour [32]. The ophthalmologist should immediately begin therapy aimed at lowering the intraocular pressure and mobilising the embolus to migrate to a peripheral vessel, hence preserving patient’s central vision [39,42].This includes administering e.g., topical timolol 0.5%, mannitol, intravenous or oral acetazolamide and performing paracentesis to lower the IOP. Intravenous steroids, e.g., methylprednisolone, may be administered to reduce the retinal edema due to ischemia [39].

To dislodge the embolus patient can be advised to repeatedly breath into a paper bag for 10 min every 30 min, which causes vasodilation, or the clinician can perform a trans palpebral ocular massage with 2 fingers or by using Goldman lens [32,39]. Furthermore, an attempt at dissolving the filler with hyaluronidase should be made, starting at the injection site, followed by the supraorbital and supratrochlear regions along with a massage to facilitate the filler’s breakdown. Peribulbar, high dose retrobulbar hyaluronidase injections and hyperbaric oxygen therapy may also be attempted, however, studies about their efficacy remain limited [32,42].

***Preventative methods***

As prevention is better than cure, methods to avert the ischemic adverse events of dermal filler injections have been outlined. These strategies include:

* proper knowledge of the periocular anatomy and safe injection points
* aspirating prior to injecting the filler to minimize the chance of an intravascular injection
* avoiding subdermal vasculature by performing injections in the mid, deep dermal or even supraperiosteal plane, depending on the filler type and manufacturer’s guidelines
* using cannulas over needles, as their blunt tip reduces the risk of vascular injury, yet remembering that they do not fully eliminate the chance of intravascular injection
* administering small volumes with slow injections using a threading or fanning technique
* manually compressing the vessel pathway when injecting near the supraorbital, supratrochlear or dorsal nasal artery to prevent retrograde flow
* incorporating doppler ultrasound to map vasculature and determine the position of the needle/cannula and its proximity to the vessels [30,32,39,42].

**DISCUSSION**

The dermal filler market is rapidly expanding, hence adequate knowledge of the products and possible adverse effects of their administration is essential among aesthetic doctors. Injections in the periocular region, especially in the tear trough, are predominantly performed for rejuvenation purposes. This area is exceptionally demanding, which requires excellent anatomical awareness of the injector, the plausible anatomical variations, safe injection points for different orbit shapes and the proper administration technique for satisfactory outcomes. The doctor’s role is to take very detailed patient’s medical history, which allows to prepare an individually adjusted treatment plan to the patient’s needs and properly select the product for the injections [1,31]. Patients ought to be informed about possible adverse effect prior to the procedure and give a fully informed consent before the injections.

Hyaluronic acid continues to be the most commonly used dermal filler, providing immediate hydration and volume for the skin, which is often used to treat the periocular region, especially tear trough deformities [1,5,6]. On top of that, it is characterized by an outstanding safety profile, especially due to its reversing agent hyaluronidase, which allows successful treatment of most post-injection complications [7]. Filler material should be carefully chosen for each procedure, bearing in mind their characteristics, durability, and indications.

For an immediate volumizing and rejuvenating effect CaHA or HA fillers should be chosen. Moreover, calcium hydroxylapatite fillers, provide an immediate brightening effect, which may be a major advantage for patients with visible venous circulation or hyperpigmentation in the periocular area [18].They are also biosynthetically produced without the use of any animal-derived product, therefore a great choice for allergy-prone patients [16]. However, they are both temporary fillers, with a durability of 6-18 months for HA and 12-18 months for CaHA fillers, therefore, patients need to repeat these procedures to maintain the results, which may be a financial obstacle for some patients and should be considered prior to choosing the filler [7,17].

Polymethyl methacrylate (Bellafill®), on the other hand, has been found to be a great long-term option for patients with dark circles and tear trough deformities as it is a permanent filler lasting up to 5 years [22,25]. Sculptra®, Radiesse®, and Bellafill® are biostimulatory fillers that encourage collagen production 4-6 weeks post-injection, which is a great benefit for rejuvenation of the periocular area, improving dermal thickness and apparent soft tissue laxity [1,13,15,23 ].In case of patients with apparent facial asymmetry, lipoatrophy or deepened scars, polyalkylimide may be the suitable filler due to its permanent nature and large volumes that can be administered by a single procedure [26].

Most adverse events after dermal filler injections are mild and resolve spontaneously without the need of medical interventions. The use of calcium hydroxylapatite, polymethyl methacrylate, poly-L-lactic acid or polyalkylimide in highly mobile structures, such as the tear trough and the periorbital region is discouraged by some researchers due to their irreversibility and an increased risk of nodule formation. This may require saline injections and redistribution of the product with massage, intralesional steroid injections or even surgical excision [1,19,36]. The most severe complications after dermal filler injections are the ischemic adverse events, including skin necrosis and vision loss, which require immediate treatment. In both cases vasodilating drugs can be administered, e.g., phosphodiesterase type-5 inhibitors, alongside hyaluronidase and topical or intravenous steroids, regardless of the filler type as they reduce edema [33,40].Hyperbaric oxygen therapy may also be attempted as adjuvant treatment [32]. Unfortunately, despite immediate treatment visual loss is often permanent, hence the need for extreme caution and adherence to preventative guidelines for vascular complications [42].

Aesthetic medicine doctors must follow preventative guidelines to minimize the risk of complications, which include aspirating before injecting the product, performing injections in the mid or deep dermal plane and administering small volumes with slow injections using a linear threading or fanning technique [32,40]. Numerous studies have shown the benefits of performing Doppler ultrasound analysis of the face to map vasculature prior to injections and determine the position of the inserted needle/cannula. Unfortunately, still only a limited number of clinicians use imaging techniques in their medical practice, which needs to change [38].

**CONCLUSION**

The dermal filler market is a continuously growing industry worth billions of dollars with the number of performed injections constantly increasing, concurrently with the amount of post-injection complications [8,33]. Thus, it is necessary to develop proper administration techniques that minimize the risk of adverse events, guidelines for preventative methods and treatment regimen.The periocular area is anatomically complex and remains challenging to treat. Although, dermal fillers are oftentimes chosen over surgical procedures due to their efficacy and remarkable safety profiles, a variety of complications can still occur [1]. The majority of adverse events are mild and transient, however, nodules, granulomas, malar edema or Tyndall effect may require prolonged and unpleasant treatment, including intralesional steroid injections, dissolving the filler using hyaluronidase or a surgical removal, which may leave the patient with a far less cosmetically pleasing result than their initial appearance [8,19]. The most severe ischemic complications may lead to irreversible damage, including skin necrosis, causing facial deformity and massive scars or even permanent vision loss [39].

Hyaluronic acid fillers have been thoroughly researched over the years, allowing to observe possible complications, developing adequate treatment algorithms and action protocols for emergencies. Moreover, imaging techniques are growing in importance allowing aesthetic doctors to significantly minimize the risk of ischemic complications and observe an increment in satisfactory patient outcomes [36,39].

The selected scientific research allows to conclude that the literature available about the remaining dermal fillers is unfortunately still limited, offering scarce guidelines in case of adverse events. Certain improvements should be implemented in this industry including, promoting research about dermal fillers other than HA and introducing a common database of the occurring complications, administered treatment and its results.

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