



Safety in the application of facial dermal fillers. Evidence Based Medicine

Seguridad en la aplicación de rellenos faciales.
Medicina basada en evidencia

Estela Vélez-Benítez, M.D.,* Jesús Cuenca-Pardo, M.D.,‡
Guillermo Ramos-Gallardo, M.D.,‡ Karina Ramos-Ramos, M.D.§

Keywords:

Dermal filler, safety, complications, adverse event.

Palabras clave:

Rellenos faciales, seguridad, complicaciones, evento adverso.

ABSTRACT

The application of facial fillers is one of the non-surgical anti-aging procedures most frequently used in doctors' offices. As with any other injectable cosmetic procedure, complications are likely to occur even in experienced hands; however, it is the duty of the plastic surgeon and dermatologist to identify them early and handle them appropriately: abscess, cellulitis, non-inflammatory nodules and foreign body granulomas are the most common complications related to the filling. The purpose of this article is to carry out a systematic literature review, propose safety guidelines to prevent complications, describe the image characteristics of the facial fillers, the complications related to the filling, interpretation problems and skin conditions that resemble complications that have to do with the filling.

RESUMEN

La aplicación de rellenos faciales es uno de los procedimientos no quirúrgicos más utilizados en el consultorio para combatir la apariencia de la edad. Como en cualquier otro procedimiento cosmético inyectable, es probable que puedan ocurrir complicaciones, incluso en manos experimentadas. Por ello, es deber del cirujano plástico y dermatólogo lograr identificarlas de manera temprana y manejarlas adecuadamente: abscesos, celulitis, nódulos no inflamatorios y granulomas de cuerpos extraños son las complicaciones más comunes relacionadas con este procedimiento. A partir de esta perspectiva, el propósito del presente trabajo es realizar una revisión sistemática para establecer los lineamientos de seguridad, prevenir las complicaciones, describir las características de imagen de los rellenos faciales y las complicaciones relacionadas con éstos, y definir los problemas de interpretación y las condiciones dermatológicas que imitan las complicaciones relacionadas con el relleno facial.

METHODOLOGY

A multidisciplinary group of the Security Committee of the Mexican Association of Plastic and Reconstructive Surgery met to discuss the management of complications associated with the use of dermal fillers. We searched for articles with meta-analysis, review, and evidence-based medicine level I and II, in English, and Spanish on MEDLINE, and PubMed and we looked up the terms «complications» and «dermal fillers».

STAGE

A 25-year-old female patient with no outstanding history, wished to have the volume of her lips increased. Hyaluronic acid was applied with an antiseptic technique with chlorhexidine, after local lidocaine with a 27 mm needle on the lower lip, application on vermilion lateral in the lower portion of the lip, aspiration of the syringe, application of 0.3 mL on each side. Immediately violet color changes were observed with progressive increase in

* Member of the security committee of the Mexican Association of Plastic, Aesthetic and Reconstructive Surgery.

‡ Advisor of the security committee of the Mexican Association of Plastic, Aesthetic and Reconstructive Surgery. FILACP Security Committee Coordinator.

§ Dermatologist of the Integral Dermatological Center in La Paz.

We declare that we have no conflict of interest.

Received:
January 24, 2019
Accepted:
March 04, 2019

volume and she referred pain. Treatment was initiated with the local application of ice and direct compression. The next day she continued to have color changes and swelling. Compressive massage, steroid with dexamethasone IM 8 mg every 24 hours for 3 days and hot water packs were indicated. After one week, there was remission and aesthetic conformity.

Topic questions in complications of facial fillings

1. What are the safety features of facial fillers?
2. What are the different types of facial fillers?
3. What are the security sites in the filler application?
4. Who are facial fillers contraindicated for?
5. How to determine the risk of complications in facial fillers?
6. When do facial filler complications occur?
7. How are complications prevented?
8. What are the main complications of facial fillers?
9. How do I make the diagnosis?
10. What is the treatment of complications?

Some useful considerations in the treatment of facial filler complications.

- What is hyaluronidase (HYAL)?
- How do I use hyaluronidase (HYAL)?
- When is antibiotic therapy indicated?
- What are the main hypersensitivity reactions?

INTRODUCTION

Fillers are used to correct expression lines, congenital or acquired soft tissue depressions, correction of post-surgical defects and for volume replacement.¹⁻⁴

Fillers are a treatment for patients seeking non-invasive rejuvenation; however, as they are used, there are more adverse effects.⁵

The American Society of Plastic Surgeons (ASPS) reports that in the USA in 2018, facial fillers were used in 810,240 patients,⁶ being the second most frequent non-surgical procedure, after the application of botulinum toxin.²

1. What are the safety features of facial fillers?

They must be safe, biocompatible, resistant to infection and easy for tissue fixation. They must maintain volume and induce minimal inflammatory reaction. They should be non-teratogenic, non-carcinogenic, non-allergenic, and should not require sensitivity tests prior to application. They ought to be: painless, cheap and stable at room temperature.^{1,7}

Recommendations: (Level of evidence III, V; recommendation C-D):

The facial filler must be safe for the patient and must comply with the safety requirements referred to in the previous paragraph. The surgeon is obliged to know these bio-safety principles.

2. What are the different types of facial fillers?

They are classified by their properties, biodegradation time, composition (one or more materials) and nature:²

- Autogenous: patient's fat.
- Biological: bovine, porcine or human collagen, hyaluronic acid (HA).
- Synthetics: paraffin, silicone, calcium hydroxyapatite (CHA), polymethylmethacrylate (PMMA), microspheres, polyacrylamide hydrogel, hydroxyethyl/ethyl methacrylate and poly-L-lactic acid (PLLA), polycaprolactone-1 (PCL-1).^{1,2}

A generic classification is divided into two main types: reversible and irreversible.⁸

According to the characteristics of the biodegradation:

- a) Temporary:
 - Rapid reabsorption < 12 months: HA and collagen.
 - Slow reabsorption < 24 months: HA with pearls of dextran, polylactic acid, calcium hydroxyapatite and polycaprolactone-1 (PCL-1).

- b) Permanent: silicone, polymethylmethacrylate and polyacrylamides.^{2,9,10}

HA fillers are the most commonly used for their safety, minimal and reversible side effects.² Their duration depends on the molecular size and their cross-linking from 12 to 18 months. There are approximately 200 types of facial fillers on the market (*Table 1*).^{1,9}

3. What are the security sites for fillers?

The body is divided into blocks composed of multiple tissues called angiosomes. Vascular accidents tend to affect these structures.¹¹ Most of the blood supply to the face is carried out through the external carotid artery. The central region of the face (eye, nose and forehead) is irrigated by the ophthalmic artery of the internal carotid in its ramifications: supraorbital, supratrochlear, nasal and lacrimal dorsal, which can be affected by injecting the glabella, nose and forehead.^{3,5}

When considering the infiltration of fillers in the temporal area, there are three potential planes for safe injection: subcutaneous, deep to the temporoparietal fascia and deep beneath the temporal muscle in the periosteum. HA fillers should be placed in the subcutaneous plane or in the depth of the temporoparietal fascia. Collagen stimulators, such as poly-L-lactic acid or calcium hydroxyapatite, should be placed deep in the temporal muscle directly in

the periosteum to provide a safe and durable volume.³

When assessing the specific risk of the site, lips are more likely to develop nodules, due to the thin mucosa, more bacterial flora and greater mobility of the perioral region. With calcium hydroxyapatite, nodules occur, HA is contraindicated in the lip mucosa. Fillers should never be injected into the muscle, especially in the orbicular due to increased nodule formation. Patients should try to minimize movement for 1 to 3 days after the procedure.¹⁰

Recommendations: (Level of evidence III-V; recommendation A):

1. Before infiltrating facial fillers, the anatomy of the face and safety sites must be known.
2. Some fillers should not be applied in some facial regions because they can form nodules.
3. Before infiltrating facial fillers, one should aspirate with the syringe and make sure that the needle is not inside a blood vessel.
4. Infiltrate bolus in small quantities and in different places.

4. Who are facial fillers contraindicated for?

Patients with hypersensitivity, bleeding disorders, severe allergies and anaphylactic shock; polymethylmethacrylate is contraindicated in the lip mucosa. Polymethylmethacrylate and poly-L-lactic acid should not be used in patients with keloid or hypertrophic scars.¹

Table 1: Types of facial fillers.

Component	Polycaprolactone	Hydroxyapatite	Poly lactic acid	Hyaluronic acid	Collagen
	Ellanse	Radiesse	Sculptra	Restylene Belotero Filorga Art Filler Juvederm Eleves Prevele Hyalform Perfectha	Zyderm Cosmoderm Cosmoplast

Recommendations: (Level of evidence III; recommendation A):

Do not use fillers in patients with hypersensitivity, bleeding disorders, severe allergies and a history of anaphylactic shock.

5. How to determine the risk of complications in facial fillers?

It is necessary to make a thorough and complete patient's medical history related to previous applications, potential symptoms of dysmorphic syndrome, allergies, reactions, autoimmune diseases, pharmacological treatments, particularly immunomodulators, chronic infections, serious diseases, family history, genetic.^{7,9}

Recommendations: (Level of evidence III, V; recommendation C-D):

1. Evaluation is essential before the procedure.
2. The complete medical history is indispensable.
3. An informed consent is mandatory.

6. When do complications of facial fillers happen?

Early complications occur in less than two weeks: related to the procedure and in response to the injected material present as erythema, bruising, hyperthermia, edema, hypersensitivity, nodules and bumps; late (14 days to 1 year) and delayed (more than 1 year). They can occur immediately up to 24 hours after the procedure; 24 hours mediation to 4 weeks and delayed more than 4 weeks.^{2,8,9,11-13}

7. How are complications prevented?

Fillers of well-known quality brands should be used, which have a lower complication rate.⁹ It is necessary to know the superficial and deep compartments between the SMAS and periosteum.¹⁴ The anatomy of the face is complex with nerves and vessels that run in thin planes. Adequate anatomical knowledge is required to avoid serious complications.³ Technical errors are related to incorrect choice, location and depth of product placement, the quantity used is not related.⁹

It is recommended to suspend immunomodulators, analgesics, anti-inflammatories and anticoagulants temporarily before treatment, avoid intense exercise for 24 hours, reinject in the same area to avoid vasodilation by lidocaine.^{1,15} The technique used is associated with the risk: the rapid injection of large volumes can cause dissection of the subepidermal plane.^{8,15}

During application, aspiration is recommended before injection. Slow application with minimal pressure at different points and small volumes (less than 0.1 mL) allows more control. Needles are moved with caution in areas prone to vascular complications. The use of blunt cannulas is recommended, allowing a deeper plane, 22 and 70 mm long caliber is recommended and the use of small needles ought to be avoided.¹⁵⁻¹⁷

A reduction in infection related to effective cutaneous antisepsis with 2% chlorhexidine gluconate, use of disposable gloves and sterile material is shown.^{15,16}

After filler application, exposure to temperature changes should be avoided for a day, touching or pressing the site and avoiding contact with water to prevent inflammation. Alcohol and tobacco consumption should be avoided for one week.^{1,15,16}

Recommendations: (Level of evidence II; recommendation B):

1. Fillers of well-known brands should be used.
2. It is mandatory to know the facial anatomy and angiosomes, as well as the application site.
3. Technical errors arise when choosing the wrong level of application and improper choice of the product.
4. Avoid rapid injection of large volumes.
5. Aspiration is recommended before filler application.
6. Avoid exposure to temperature changes, pressing the site, drinking alcohol and smoking cigarettes for one week.
7. Suspend anticoagulants and intense exercise for 24 hours. Avoid reinjections in the same areas.
8. Avoid applying large bolus. Slow application of small volumes is recommended.
9. Use blunt cannulas for application.

10. Carry out effective cutaneous antisepsis with 2% chlorhexidine gluconate, use of sterile disposable gloves and sterile material.

8. What are the main complications that occur?

The most common are abscess, cellulite, non-inflammatory nodules and granulomas. The least frequent: infection, vascular lesion and blindness (Table 2).^{2,4}

Edema, ecchymosis and erythema appear at the time of infiltration and resolve spontaneously if a hypersensitivity reaction is persistent. Patients with rosacea are at greater risk.¹

Nodules are frequent. Those inflammatory can appear from days to years and those non-inflammatory show up after infiltration and are related to incorrect placement.¹³

By their presentation: cystic, edematous and sclerosing. They are palpable, well-defined at the injection site, caused by the application of abundant material, accumulation or displacement by the movement of the muscles.¹⁵

Infection, rare incidence of < 0.2%, due to inadequate asepsis of the skin, related to *Staphylococcus epidermidis*, *Propionibacterium acnes* and non-tuberculous mycobacteria (MNT), presentation of 3-6 weeks.² Being able to form an abscess.

Migration result of displacement by the muscles or the severity of the filling, superficial planes or in mobile anatomical areas, such as lips.¹

Granuloma, the encapsulated filling can resist degradation and remain sequestered in macrophages, secreting cytokines that attract other macrophages, increasing in size or merging into a granuloma, with histopathological criteria, unlike the nodule. The frequency is 0.01 to 1%, present in all fillers after months and up to years. However, a high incidence with polycaprolactone is reported.⁹ They appear as inflamed red nodules with negative culture.^{1,16}

Biofilm, accumulations of microorganisms that adhere to each other on a variety of surfaces. Bacteria can prevent the autoimmune reaction; consequently, antibiotics have no effect.¹⁸

Vascular infarction and necrosis, one of the most severe complications. It occurs in

Table 2: Classification of complications in fillers.

Early reactions
Vascular infarction/soft-necrosis
Acute and chronic inflammatory reactions
Infection
Allergic reactions/hypersensitivity
Symptoms of infection
Pain
Ecchymosis
Erythema
Bleeding
Inappropriate placement
Distant Propagation
Late reactions
Inflammatory reaction (acute or chronic)
Infection
Granulomas (typically chronic)
Differential diagnosis
Nodules
Depigmentation
Filler offset

the immediate phase, owing to intravascular embolism of the injected material, direct needle injury or external compression of the vasculature due to the hydrophilic properties of the product.¹ One of the most devastating complications producing localized skin necrosis or permanent loss of vision due to ophthalmic artery involvement. Lesion of the artery of the retina can cause vascular occlusion in the retina.^{8,16} Arterial embolization is commonly antegrade, with direct occlusion of an artery causing ischemia distal to the injection site. Retrograde flow of the filler against blood pressure followed by an antegrade flow through the arterial branch causes drug embolism (Freudenthal-Nicolau syndrome).¹⁷ Due to the vascular nature, glabella is the most frequent site of necrosis caused by intra-arterial injection,^{16,17,19} followed by the nasal region, nasolabial fold and forehead. Involuntary injections of the nasal, supratrochlear, angular and dorsal artery can cause ischemia and necrosis.^{1,20} Most cases are caused by fat infiltration followed by hyaluronic

acid.⁵ Clinically they manifest themselves with pain and ischemic paleness,^{5,16} immediate changes: whitening, color changes, pain (except for the presence of nerve block or local anesthesia), slow or absent capillary filling, loss of function and finally skin necrosis.¹ A venous occlusion happens with a veined mottle called *livedo reticularis*.¹⁶

9. How do I make the diagnosis?

In most cases, injectable facial fillers are detected incidentally in cross-sectional imaging studies. Magnetic resonance imaging (MRI) or high definition ultrasound detects the location and volume of injected facial fillers, evaluating related complications. MRI is preferred over ultrasound by providing anatomical reference. CT does not offer advantages over MRI.^{2,21} Paraffin as a facial filler causes severe granulomatous reactions and «paraffinoma formation». The characteristics of the CT for «paraffinoma» include rounded foci and soft tissue density nodules with a calcified edge.²

Recommendations: (Level of evidence I-III; recommendation A-B):

1. To locate the location and volume of injected facial fillers, evaluating related complications requires magnetic resonance imaging (MRI) or high definition ultrasound.
2. MRI provides anatomical references.
3. CT does not offer advantages.

10. What is the treatment of complications?

The treatment depends on the severity. Frequently, it can be self-limited and resolved spontaneously in hours or days. Some cases require local and systemic treatment. The nature of the complication is classified as mild and disappears by itself, moderate and require treatment, or severe in need of immediate intervention.^{2,9}

Edema, ecchymosis and erythema, resolves spontaneously, with cold, massage and antihistamines; if it persists for several days, steroid and vitamin K are necessary.¹

Measures to avoid nodules, granulomas and migration are recommended for deep plane

infiltration and firm massage. Those related by poly lactic acid are more persistent and difficult to treat, responding to intralesional steroids. The management of the cystic type nodule is incision and drainage. Steroids are less effective for calcium hydroxyapatite.²²

Complicated cases with infectious processes require biopsy cultures and specific treatment.^{1,8,15} In case of fluctuating abscess, an incision and drainage is required. If it does not fluctuate, antibiotics and steroids are recommended. Hyaluronidase should not be used because of the risk of spreading the infection. If these treatments fail, biofilm formation by methicillin-resistant *Staphylococcus aureus* (MRSA) or atypical tuberculosis (TB) should be suspected.^{1,8} Once the signs of infection have disappeared, hyaluronidase can be used to decrease fibrosis.^{15,23} Hyaluronidase helps break down the biofilm matrix, reducing the size. Other options are prolonged antibiotic therapy, the administration of intralesional 5-FU and intralesional laser.^{1,8,16,24} Surgical preparation and a good sterile technique can reduce its incidence.⁸

In the case of suspected necrosis, treatment should be started immediately. The injection should be stopped; pressure and massage should be applied to the area, warmth or warm compresses should be used to increase vasodilation. The goal of treatment is to dissolve the product, facilitate blood flow and promote vasodilation. Topical nitroglycerin (1%), hyaluronidase, aspirin and systemic or topical steroids are suggested to reduce inflammation and the degree of injury.^{1,8,15,16} However, some authors mention that nitroglycerin can make ischemia worse. Aspirin, intravenous prostaglandins, puncture filler removal and low molecular weight heparin have not proven to be effective.^{1,16} Some authors recommend the use of hyaluronidase in all cases of vascular compromise, regardless of the type of filling, to reduce edema and pressure in the occluded vessel. After the initial treatment, if ischemia persists, hyperbaric oxygen is put forward; however, evidence is not strong enough to support this recommendation.¹¹ In case of necrosis, debridement is required and reconstruction with skin graft or cartilage and local flaps.^{1,15}

For intravascular infarction, a minimum of 200 to 300 U of hyaluronidase per day is recommended throughout the necrotized area, for a minimum of two days until signs of blood flow appear (if necessary up to 1500 U). The patient must be reevaluated every 24 hours. If an infection appears, antibiotic therapy should be initiated. There is uncertainty of treatment in cases of blindness; however, immediate injection of hyaluronidase is recommended.^{23,25}

Measures to improve the retinal perfusion described, with limited results include: immediate ophthalmologic consultation, eye massage, ophthalmic drops with timolol, hyperbaric therapy, diuretics, systemic and topical corticosteroids, anticoagulation and decompression of the anterior chamber.^{15,21}

Late reactions resolve, and oral steroids are required.¹⁶ Pulsed light is indicated in the treatment of hypertrophic scar and telangiectasias.¹

Recommendations: (Level of evidence III, V; recommendation A-B):

1. The treatment depends on the severity. Frequently, it can be self-limited and resolved spontaneously.
2. Edema, ecchymosis and erythema, resolves spontaneously, with cold, massage and antihistamines.
3. In case of infection or fluctuating abscess, culture, antibiotics, incision and drainage are needed. If it does not fluctuate, antibiotics and steroids are recommended. In the initial stage, hyaluronidase should not be used due to the risk of spreading.
4. If the diagnosis is necrosis, treatment is immediate.
5. For intravascular infarction, a minimum of 200 to 300 U of hyaluronidase per day is recommended throughout the necrotized area for a minimum of two days until signs of blood flow appear; if necessary up to 1500 U.
6. It is necessary to have an emergency kit in the office (*Table 3*).

Some useful considerations in the treatment of facial filler complications

What is hyaluronidase (HYAL)?

It is a mucolytic enzyme that hydrolyzes the natural and cross-linked dermal fillers of HA, being the gold standard for the treatment of complications associated with HA filling.^{6,26}

Three main groups of adverse effects due to HA fillers are treated with hyaluronidase: excessive or superficial application, nodules and vascular occlusions.²³

How do I use Hyaluronidase (HYAL)?

During the first six hours, 0.08 mL of each product with 16 units of hyaluronidase with a degradation of 90% is recommended. Washing the ischemic tissue with hyaluronidase can replace direct intravascular injection in most cases.²³

Hyaluronidases dosage by region of application in nasal and perioral skin: 15-30 units, 30 units in periorbital area; 10-15 units in infraorbital area and 1.5 units in the lower eyelid.²⁷

Recommendations for hyaluronidase:

- Area < 2.5 mm: simple 10-20 U injection.
- mm - 1 cm: 2-4 injection points with 10-20 U per injection.
- Injections can be repeated daily and for at least 4 days.²⁸

The different HA gels differ in their sensitivity to hyaluronidase. The use of

Table 3: Components of the hyaluronic acid filler complication management kit.

Hyaluronidase
Steroids: oral and intralesional
Antibiotics
Antivirals
1% topical nitroglycerin
Antihistamines
Aspirin 325 mg orally
Warm compresses
Emergency ophthalmologist and hyperbaric oxygen telephone

higher doses for more resistant fillers and in emergency situations is considered.²³ Serious hypersensitivity reactions to hyaluronidase are possible; but, so far, they have not been reported.^{23,28}

Recommendations: (Level of evidence I-IV; recommendation A):

1. The recommended dose is 0.08 mL of each product with 16 units of hyaluronidase with a degradation of more than 90% within 6 hours of exposure.
2. The different HA gels differ in their sensitivity to hyaluronidase. The use of higher doses for more resistant fillers and in emergency situations is considered.²³

When is antibiotic therapy recommended?

Initial empirical antibiotic therapy is recommended, followed by a reassessment if there is no improvement, with biopsy and culture, indicating clarithromycin 500 mg plus moxifloxacin 400 mg twice a day for 10 days, or ciprofloxacin 500 to 750 mg twice daily for 2 to 4 weeks, or minocycline 100 mg once daily for 6 months.¹⁵

In early acute infections: amoxicillin + clavulanate, cephalexin, or ciprofloxacin and continue with hyaluronidase and steroids. In late chronic infections a sequence is indicated: third or fourth generation (empirical) cephalosporin antibiotics (cefixime), hyaluronidase, and steroids.¹⁵

To avoid recurrent herpetic outbreaks, antiviral prophylaxis is recommended in patients with herpes and should be delayed until complete resolution.¹⁵

In cases of methicillin-resistant *Staphylococcus aureus* (MRSA) or atypical tuberculosis (TB),^{1,8} culture of infected material, TB test, quinolones, macrolides or third generation cephalosporin, hyaluronidase, 5-FU and a final resection.^{1,16}

Recommendations: (Level of evidence III-V; recommendation A-C):

1. Initial empirical antibiotic therapy is recommended.
2. Clarithromycin 500 mg plus moxifloxacin 400 mg twice a day for 10 days, or

ciprofloxacin 500 to 750 mg twice daily for 2 to 4 weeks, or minocycline 100 mg once daily for 6 months.

3. Early acute infections: amoxicillin + clavulanate, cephalexin, or ciprofloxacin, and continue with hyaluronidase and steroids.
4. Late chronic infections a sequence is indicated: third or fourth generation (empirical) cephalosporin antibiotics (cefixime), hyaluronidase, and steroids.

What are the main hypersensitivity reactions?

They are related to microbial contamination, recommending broad-spectrum antibiotics, avoiding steroids and NSAIDs.²⁴

From an immunological perspective, fillers act as adjuvants rather than direct activators of T cells, with a genetic predisposition. The management of acute and systemic reactions is usually difficult, requiring anti-inflammatory and immunosuppressive therapy.¹³

Progressive angioedema should be considered an emergency due to a possible airway obstruction.¹⁵

Initially, with HA there was hypersensitivity and granulomas. However, they are now rare (multiform rash and anaphylaxis), when applied very superficially, the Tyndall effect with a «bluish» discoloration occurs, they are usually short-lived and respond to hyaluronidase.^{8,9,29}

Recommendations: (Level of evidence I, III-V; recommendation A-B):

In allergic or hypersensitive reactions, broad-spectrum antibiotic therapy is recommended, and steroids and NSAIDs should be avoided.

DISCUSSION

The safety committee provides information about fillers and their complications, which can help doctors, allowing them to successfully avoid and treat possible adverse effects.

Filler injection for soft tissue augmentation is a satisfactory procedure with very modest results, despite having high expectations. However, as the number of indications and performance increases, the number of complications also increases. It is important

that doctors know the facial anatomy and high-risk areas.

Lack of experience is a factor contributing to the development of complications.

The doctor who injects the filler should have broad experience to avoid serious errors at the injection site, volume, speed, depth, as well as post-injection treatment. The doctor should be available after the injection and never underestimate the concerns of a patient.⁹

Proper product selection, adequate techniques to minimize adverse reactions, thorough knowledge of the anatomy obtain a complete medical history and a history of relative or absolute contraindications. Postsurgical changes; for example: rhinoplasty where in the vast majority of cases, they show a change in vascularization and fibrosis of certain areas.^{4,8,15,30,31}

The ophthalmic artery is significantly associated with irreversible blindness. Unilateral blindness is the most frequent adverse vascular effect; autologous fat tends to cause more cases of permanent vascular damage.^{19,20,32,33}

Precautions according to the Global Aesthetic consensus to avoid intravascular injury include aspiration before injection, slow injection with minimal pressure and the supply of material at different points and in small volumes. It is important to keep the needle moving. The use of small needles has been recommended by some authors and blunt microcannulas have been recommended.¹⁵

Treating a patient with empathy has avoided many legal demands,⁹ early identification and correct treatment allow the successful resolution of inflammatory symptoms in a few days.³⁴

The doctor's technique is the most important with regard to safety.¹

CONCLUSIONS

Doctors should be fully aware of the signs and symptoms related to complications and are prepared to treat them with confidence. The establishment of emergency action protocols, with agents readily available in the office, would reduce the severity of adverse outcomes associated with the injection of hyaluronic acid fillers in the cosmetic environment.

This document seeks to establish a set of recommendations and identify key problems that may be useful for doctors who are beginning to use dermal fillers. In addition, this document provides a better understanding of the diagnoses and management of complications if they occur.

Cheap products not tested should never be used.

REFERENCES

1. Joo Hyun Kim, Duk Kyun Ahn, Hii Sun Jeong, and In Suck Suh. Treatment algorithm of complications after filler injection: based on wound healing process. *J Korean Med Sci* 2014; 29 (3): 176-182.
2. Mundada P, Kohler R, Boudabbous S, Toutous Trelu L, Platon A. Injectable facial fillers: imaging features, complications, and diagnostic pitfalls at MRI and PET CT. *Insights Imaging* 2017; 8 (6): 557-572.
3. Breithaupt AD, Jones DH, Braz A, Narins R, Weinkle S. Anatomical basis for safe and effective volumization of the temple. *Dermatol Surg* 2015 Dec; 41, 1: S278-83
4. Bruna Souza FB, Gonçalves Bravo L, Da Rocha CM, Bianco de Souza S, Lopes FL. Evaluation and Proportion in Nasal Filling with Hyaluronic Acid. *J Clin Aesthet Dermatol* 2018; 11 (4): 36-40.
5. Beleznay K, Carruthers JD, Humphrey S, Jones D. Avoiding and treating blindness from fillers: A review of the World Literature. *Dermatol Surg* 2015; 41 (10): 1097-117.
6. The American Society for Aesthetic Plastic Surgery. *Cosmetic (Aesthetic) Surgery National Data Bank*. The American Society for Aesthetic Plastic Surgery, 2018. Disponible en: https://www.surgery.org/sites/default/files/ASAPS-Stats2018_0.pdf
7. Urdiales-Gálvez F, Delgado NE, Figueiredo V, Lajo-Plaza JV, Mira M. Preventing the Complications Associated with the Use of Dermal Fillers in Facial Aesthetic Procedures: An Expert Group Consensus Report. *Aesthetic Plast Surg* 2017; 41 (3): 667-677.
8. DeLorenzi C. Complications of injectable fillers, part 2: vascular complications. *Aesthet Surg J* 2014; 34 (4): 584-600.
9. Haneke Eckart. Adverse Effects of Fillers and Their Histopathology. *Facial Plast Surg* 2014; 30: 599-614.
10. Ledon JA, Savas JA, Yang S, Franca K, Camacho I, Nouri K. Inflammatory nodules following soft tissue filler use: a review of causative agents, pathology and treatment options. *Am J Clin Dermatol* 2013; 14 (5): 401-11.
11. Rohrich RJ, Nguyen AT, Kenkel JM. Lexicon for soft tissue implants. *Dermatol Surg* 2009; 35 (Suppl 2): 1605-1611.
12. Urdiales-Gálvez F, Delgado NE, Figueiredo V, Lajo-Plaza JV, Mira M. Treatment of Soft Tissue Filler Complications: Expert Consensus Recommendations. *Aesthetic Plast Surg* 2018 Apr; 42 (2): 498-510.
13. Alijotas-Reig J, Fernandez-Figueras MT, Puig L. Inflammatory, immune-mediated adverse reactions related to soft tissue dermal fillers. *Semin Arthritis Rheum* 2013; 43 (2): 241-58.

14. Rohrich RJ, Pessa JE. The fat compartments of the face: anatomy and clinical implications for cosmetic surgery. *Plast Reconstr Surg* 2007; 119 (7): 2219-2227.
15. Signorini M, Liew S, Sundaram H, De Boule KL, Goodman CJ, Monheit G, Wu Y, Trindade de Almeida AR, Swift A, Vieira Braz A; Global Aesthetics Consensus Group. Global Aesthetics Consensus: Avoidance and Management of Complications from Hyaluronic Acid Fillers-Evidence- and Opinion-Based Review and Consensus Recommendations. *Plast Reconstr Surg* 2016; 137 (6): 961e-71e.
16. Woodward J. Facial Filler Complications. *Facial Plast Surg Clin North Am* 2015; 23 (4): 447-58.
17. Dayan SH. Complications from toxins and fillers in the dermatology clinic: recognition, prevention, and treatment. *Facial Plast Surg Clin North Am* 2013; 21 (4): 663-73.
18. Ibrahim O, Overman J, Arndt KA, Dover JS. Filler Nodules: Inflammatory or Infectious? A Review of Biofilms and Their Implications on Clinical Practice. *Dermatol Surg* 2018; 44 (1): 53-60.
19. Sito G, Manzoni V, Sommariva R. Vascular Complications after Facial Filler Injection: A Literature Review and Meta-analysis. *J Clin Aesthet Dermatol* 2019; 12 (6): E65-E72.
20. Thanasarnaksorn W, Cotofana S, Rudolph C, Kraissak P, Chanasumon N, Suwanchinda A. Severe vision loss caused by cosmetic filler augmentation: Case series with review of cause and therapy. *J Cosmet Dermatol* 2018; 17 (5): 712-718.
21. Ginat DT, Schatz CJ. Imaging Features of Midface Injectable Fillers and Associated Complications. *Am J Neuroradiol* 2013; 34 (8): 1488-1495.
22. Kadouch JA. Calcium hydroxyapatite: A review on safety and complications. *J Cosmet Dermatol* 2017; 16 (2): 152-161.
23. Landau M. Hyaluronidase Caveats in Treating Filler Complications. *Dermatol Surg* 2015; 41 (Suppl 1): S347-53.
24. Dumitraşcu DI, Georgescu AV Clujul Med. The management of biofilm formation after hyaluronic acid gel filler injections: a review. *Clujul Medical* (1957) [05 Aug 2013, 86 (3): 192-195].
25. Buhren BA, Schrupf H, Bölke E, Kammers K, Gerber PA. Standardized in vitro analysis of the degradability of hyaluronic acid fillers by hyaluronidase. *Eur J Med Res* 2018; 23 (1): 37.
26. Cavallini M, Gazzola R, Metalla M, Vaienti L. The role of hyaluronidase in the treatment of complications from hyaluronic acid dermal fillers. *Aesthet Surg J* 2013; 33 (8): 1167-74.
27. Buhren BA, Schrupf H, Hoff NP, Bölke E, Hilton S, Gerber PA. Hyaluronidase: from clinical applications to molecular and cellular mechanisms. *Eur J Med Res* 2016; 21: 5
28. Rayess HM, Svider PF, Hanba C, Patel VS, DeJoseph LM, Carron M, Zuliani GF. A Cross-sectional Analysis of Adverse Events and Litigation for Injectable Fillers. *JAMA Facial Plast Surg* 2018; 20 (3): 207-214.
29. Haneke E. Adverse effects of fillers. *Dermatol Ther* 2019; 32 (2): e12676.
30. Robati RM, Moeineddin F, Almasi-Nasrabadi M. The Risk of Skin Necrosis Following Hyaluronic Acid Filler Injection in Patients with a History of Cosmetic Rhinoplasty. *Aesthet Surg J* 2018; 38 (8): 883-888.
31. Bertossi D, Giampaoli G, Verner I, Pirayesh A, Nocini R, Nocini P. Complications and management after a nonsurgical rhinoplasty: A literature review. *Dermatol Ther* 2019; 32 (4): e12978.
32. Fitzgerald R, Bertucci V, Sykes JM, Duplechain JK. Adverse Reactions to Injectable Fillers. *Facial Plast Surg* 2016; 32 (5): 532-55.
33. Murthy R, Roos JCP, Goldberg RA. Periocular hyaluronic acid fillers: applications, implications, complications. *Curr Opin Ophthalmol* 2019; 30 (5): 395-400.
34. Bhojani-Lynch T. Late-Onset Inflammatory Response to Hyaluronic Acid Dermal Fillers. *Plast Reconstr Surg Glob Open* 2017; 5 (12): e1532.

Correspondence:**Estela Vélez Benítez, M.D.**

Flamencos No. 74,

Col. San José Insurgentes,

Alcaldía Benito Juárez, 03900,

Mexico City, Mexico.

E-mail: cirugiaplastica@draestelavelez.com