

Poly-L-lactic acid: a biostimulating agent

Ácido Poli-L-Láctico: um agente bioestimulador

ABSTRACT

Poly-L-lactic acid (PLLA) is a biocompatible, re-absorbable, immunologically inert polymer that induces neocollagenesis through a subclinical inflammatory response. It is indicated for restoration of facial volume associated with facial lipoatrophy in immunocompetent or HIV-immunodeficient patients. In addition there are cosmetic indications for extra facial areas. For more than three decades it has been used in medical devices such as plates, screws, intraosseous and soft tissue implants, and as a biodegradable vector for drugs, in sutures and stents. The present article is aimed at presenting a literature review on the indications, application method, and complications of the use of PLLA.

Keywords: collagen; skin aging; rejuvenation

RESUMO

O ácido poli-L-láctico (PLLA) é polímero biocompatível, reabsorvível, imunologicamente inerte, que induz a neocolagênese através de resposta inflamatória subclínica, indicado para restauração do volume facial associado à lipoatrofia facial em pacientes imunocompetentes ou com imunodeficiência pelo vírus HIV, além das indicações cosméticas em áreas extrafaciais. Há mais de três décadas vem sendo usado em dispositivos médicos como placas, parafusos, implantes intraósseos, de tecidos moles, como vetor biodegradável para medicamentos, em fios de sutura e stents. Este artigo tem como objetivo apresentar uma revisão da literatura sobre indicações ao uso do PLLA, seu modo de aplicação e suas possíveis complicações.

Palavras-chave: colágeno; envelhecimento da pele; rejuvenescimento.

INTRODUCTION

The facial aging process starts slowly at around the age of 20, when the cell renewal rate slows down.¹ Nevertheless, the visible manifestations take years to be noticed and are determined by the depression of soft tissues, with the loss of muscle, subcutaneous and osseous tissues, and skin atrophy.^{2,3}

Minimally invasive techniques for facial rejuvenation are performed with cutaneous fillers, volumizers, and enhancers,⁴⁻⁶ and are a good option for many patients. Currently, cutaneous fillers can be classified into two categories: temporary or biodegradable products (which persist for months or a few years) and non-resorbable or permanent products.⁷ Considering that the aging process is continuous, temporary fillers should be preferred.²

Poly-L-lactic acid (PLLA) was approved as a cutaneous filler in Europe in 1999, under the trade name of New-Fill.⁸ In 2004 it was approved by the FDA in the U.S. with the brand name Sculptra (Dermik Laboratories, Sanofi Aventis, USA), for the treatment of HIV-associated lipoatrophy and for treating volume loss with an aesthetic purpose in 2009,⁸⁻¹¹ under the name Sculptra Aesthetic (Sanofi Aventis).^{12,13} By 2006 over 150,000 patients had been treated^{14,15} in more than 30 countries.¹⁶

Review article

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The PLLA is a synthetic molecule discovered by the Centre National de la Recherche Scientifique (CNRS), Lyon, France, in 1954. It is derived from lactic acid, which is naturally produced by muscle contraction. The product is marketed as a lyophilised powder in a sterile vial containing non-pyrogenic mannitol, sodium croscarmellose and microparticles of PLLA (97.5% of water)¹⁷ measuring 40–63 microns in diameter and belonging to the family of alpha-hydroxy acids^{13,18} produced from the fermentation of corn.¹² The size of the particles prevents them from being phagocytized by macrophages in the dermis or from passing through the walls of capillaries. Nonetheless, they are small enough to be injected with a 26G needle.¹³

The mechanism of action occurs through the stimulation of fibroblasts^{4,13,15} in response to a subclinical tissular inflammation. It is this fibroplasia that produces the desired cosmetic result.¹³ New collagen begins to form after one month and continues to increase for nine months to a year. In the sixth month many particles become porous and surrounded by macrophages. After this period there is no evidence of fibrosis and the PLLA particles disappear.^{6,19} The product's degradation occurs through non-enzymatic hydrolysis into lactic acid monomers that are metabolized into CO₂, H₂O or incorporated into glucose.^{1,14,16} With its half-life estimated at 31 days, PLLA is totally eliminated from the body in about 18 months.²⁰

An increase of 4 to 6mm in the thickness of the dermis 5 has been demonstrated through Doppler ultrasound, evidencing the presence of support in the skin for 96 months.⁶ An ultrasound study measured the skin thickness of 33 patients with HIV-associated lipoatrophy who were treated with 4 sessions of PLLA and showed a 151% increase in skin thickness at 12 months and a 196% increase at 24 months, confirming that the effect of neocollagenesis continues several months after the injection of the product.²¹ Vega, Westminster, Blue Pacific and Apex, and, more recently Fitzgerald and Vleggaar,¹³ and Rendon 21 have repeatedly demonstrated through prospective clinical studies that the duration of clinical effects may be two years or more.

The best indication for the product is to use it as three-dimensional biostimulator 1,20 in patients seeking a natural look without the appearance of tiredness.¹³ The PLLA is not injected directly into wrinkles or furrows, but diffusely in areas that are concave or in areas of shadow, caused by hypodermic and/or subcutaneous fat loss due to aging, weight loss, trauma, lipoatrophy secondary to diseases,¹⁹ corticosteroid injection, and after facelift surgery.²²

The use of PLLA should be avoided in certain facial areas, such as perioral and periorbital regions,^{5,16} which are regions of muscle hypermobility,²³ and it is not indicated for filling the lips.^{5,16} It promotes the improvement of facial contour, including jaw lines, nasolabial folds, temporal region, malar region¹⁵ and the correction of marionette lines, and restores the harmonic shape of the face.

In 2009, Sadick and Palmisano 24 reported the case of a 60-year-old woman with acne scars who underwent several previous procedures, with success after seven PLLA sessions, corroborating a study by Beer,²⁵ who published the follow-up of 16

cases of moderate and severe acne scars²⁴ and varicella scars, with a significant reduction measured in distensible scars (2–3mm) after a similar number of sessions. Grimald et al. used the product in three sessions with the aim of increasing the thickness of the skin in a patient bearer of Parry-Romberg syndrome, in a procedure that followed the Coleman technique to reconstruct the three-dimensional projection of the face²⁶ or areas of asymmetry, as referred by Burgess.¹⁴ Other areas have been treated, including the neck,²¹ hands,^{27–29} breast,^{16,30} and atrophic scars.

Coimbra and Amorim³¹ obtained good results with the sagging of arms in 16 women after treatment with PLLA.

It is worth noting that Vleggaar improved the appearance and contour of a patient with pectus excavatum³² with three PLLA sessions, and Shulman et al. described the correction of thoracic deformity secondary to breast reconstruction after mastectomy, in a thin 63-year-old woman. The step formed between the implant and the skin was corrected with two vials per session, totaling four sessions.³³ Hamilton and Burgess published a discussion on the use of the product in melanodermic patients (Fitzpatrick IV to VI), with modifications of the technique—such as extended time between sessions and the injection of the product in different layers, like the subcutaneous, and small amounts over the bone of the maxilla and zygoma—achieving better aesthetic results.³⁴ The procedure proved to be safe in those patients.

The contraindications to the use of the product are: areas previously treated with permanent fillers such as silicone or polymethylmethacrylate,^{3,11,20} and patients on aspirin, vitamin E, fish oil capsules, non steroidal antinflammatories and anticoagulants, the latter which should be discontinued ten days before the procedure.^{3,5,27} The use of PLLA is also not approved in children, and pregnant or lactating women.³ Other contraindications are: use of immunosuppressants, heavy smoking, and patients eager for immediate results. Patients with chronic use of immunosuppressants and anti-inflammatory drugs such as corticosteroids, should be treated with extreme caution, for suppressing the inflammatory response during the treatment with prednisone can lead to subtherapeutic response. After discontinuing or interrupting prednisone, an exaggerated response to PLLA may occur.²²

The reconstitution of the product should be performed in distilled water (DW), ranging from 2¹³ to 24 hours,^{22,25} or even 72 hours before use^{5,19} (which would facilitate the dilution), or up to seven days if diluted in DW with bactericidal, according to Palm.¹¹ Lam et al. emphasized that reconstructions of less than 12 hours increase the risk of nodules.¹⁶

Initially, the laboratory that manufactured New-Fill suggested dilution of the product in 3 ml of DW,²³ carried out 30 minutes prior to use, 3 which would imply greater risk of adverse effects.¹⁸ Currently, other dilutions can be used, such as in five,^{2,4,5,11,14,23,25} six,^{22,34,35} seven,^{5,8,11,12} eight²⁹ or 12ml,²⁷ supplemented or not with 1% or 2% lidocaine 32 of 1–4ml per vial. After hydrating the PLLA, the vials must be kept at rest up until the moment of use, preventing the deposition of particle agglomerates on their wall.¹³ Since 2004, Rendon²² dilutes in saline solution associated with lidocaine, providing a tumescent anesthetic effect and decreasing the discomfort, with a final volume of 6–8ml,^{5,20}

with dilutions lower than 10ml being used in the face,^{5,22} and of up to 16ml^{11,31} or 20ml³¹ in extrafacial areas. Immediately before use, the product should be shaken vigorously in order to obtain a homogeneous suspension with few bubbles.

The stability of the product after reconstitution at room temperature is 72 hours,^{5,16} although Sherman²² believes that dilution in DW plus bactericidal allows its use within up to 30 days.^{19,22}

For the application, skin antisepsis must be carried out with chlorhexidine, applying 4% lidocaine 30 minutes before.^{4,22} Some authors carry out infraorbital nerve block with lidocaine,^{6,14,34} in addition to mentonian nerves.^{19,34} Sherman²² applies ice packs before and after the injection of PLLA to decrease pain, stimulate vasoconstriction and reduce the formation of hematoma and echymosis. Pain is felt as the needle perforates the dermis or touches the periosteum. Fabi¹¹ and Goldman¹² treated 90 cases only with 1% lidocaine with 1:100,000 epinephrine, added to the solution.

Due to the fact that it is a procedure performed in series, with benefits gradually increasing over months, it is important to record the development with photographs (frontal, lateral, and oblique).¹⁹ The area to be treated should be mapped in such a way that the areas in which applications will be carried out are identified. Convex areas should be marked in order not to be filled.²²

The application technique consists of using a 1 to 3ml syringe and an 18G needle to withdraw the product from the vial. The needle used in the application itself is a 26G, with the product being applied between the deep dermis and hypodermis. Prior aspiration is carried out to avoid intravascular injection, with an entry angle into the skin of between 30° and 45°, with 0.1–0.2 ml of the product being slowly deposited in retroinjection. In order to prevent superficial deposits, which may cause the emergence of papules, the injection should be halted when $\frac{3}{4}$ of the needle becomes apparent.²² The PLLA is applied in parallel lines or in the shape of an “X”. The technique of filling in small bolus is employed in areas of very thin skin—such as the temples—in small volumes of 0.05ml, nevertheless the formation of nodules may take place.²² According to Sherman,²² the application should be implemented at a continuous pace and with continuous movement during the retroinjection, in order to prevent the deposition of bolus, which depending on the depth, can lead to the formation of papules or nodules. This observation is especially important for those with a beginner skill level for applying the product, who should always carry out aspiration before injection.²² For areas of very thin skin, Sherman also prefers the tunneling technique, applying the product in small amounts, depositing between 0.025 and 0.05 ml, above the periosteum. For those who are already skilled in handling the product, he suggests applications in the shape of fans, consisting of multiple retrograde tunnels with few punctures to cover larger areas, such as the genian, pre-auricular, and mentum’s lateral regions, nasogenian sulci, and the lateral region of the eyebrows.¹⁹

The treated area should be massaged immediately after the application in order to ensure an even distribution of the product. The application of ice at the site stimulates vasoconstriction and prevents echymosis. The syringe must be kept parallel to the skin’s surface during application, which keeps the needle pervious during

the procedure. The use of 3ml syringes with a content of 1ml makes for comfortable handling and allows its manipulation in a way that prevents the precipitation of PLLA and avoids the clogging of the needle.²² Sherman still advises that the direction of the application of the product should be from top to bottom and from medial to lateral, in the face. The face must be treated globally, rather than filling only the cavities, thereby avoiding overcorrection.^{3,13,16}

The application technique of PLLA varies according to each author’s experience. Lowe et al.⁴ published a retrospective study of 281 treated cases, where 0.05 ml of PLLA were deposited in the deep dermis or upper subcutaneous using tunneling retroinjection, in the shape of an “X” or that of a fan.⁶ According to Beer,¹⁵ this cross technique ensures better distribution of the product in the desired plane. Lam et al.¹⁶ suggest that the “X” technique allows a better distribution of the product in addition to the fact that its application in the subcutaneous minimizes the risk of complications. They treat infraorbital and temporal areas with transcutaneous bolus 5 of 0.1ml per deposit in a dilution of 11ml. Lacombe^{8,9} recommends that the application in the infraorbital margin be carried out with a long needle into the lateral of the orbit in small deposits, avoiding echymosis and the surfacing of the product across the muscle. For the lower half of the face he uses a long needle and application in the shape of fans⁸ or an “X” in order to reduce the number of punctures. Fitzgerald and Vleggaar’s treatment protocol¹³ consists of carrying out the applications in the deep subcutaneous in the medial region of the cheeks and mentum, and in the superficial subcutaneous in the parotid and masseteric region, with the “X” or fan shape technique or using 0.1–0.3 ml/cm, in addition to suprapariosteal applications in the zygoma, maxilla, and mandible using 0.2–0.3 ml/cm. In the temporal region, the protocol recommends applying 0.3–0.5 ml/cm deposits of the product.

Palm and Chayavichitsilp¹¹ described modifications of the techniques used. Suprapariosteal injections in the temporal region, piriform aperture, zygoma and canine fossa, and bolus in the anterior mandibular sulcus. It is important to note that the application in the piriform aperture and mentum region is performed through intraoral access. They also perform PLLA applications in the bottom of the superior and inferior gingival sulcus. The authors claim to have been performing that technique for five years without any complication. When applying the product in the infraorbital margin, the needle is oriented from the genian region towards the orbit. The remainder is applied using the fan technique, as described above. Good results were reported by Hamilton and Burgess,³⁴ after application in different layers of the skin aimed at an adequate restoration of facial volume, resulting in a more youthful appearance. Small boluses are applied over the bone in the maxilla and zygoma, starting in the nasofacial sulcus. With the correction of the malar region, other regions of the maxilla also improve, with the application carried in the deep subcutaneous tissue.

Sadick et al.²⁷ treated the hands of 26 patients with subdermal and above-the-facial-plane deposits of 0.3–0.5ml, with 8–10ml dilutions. Coimbra and Amorim³¹ published the report of a treatment in the medial region of the arms of 22 women,

where the linear retrograde technique was applied, with a dilution of 20ml and deposits of 0.05ml per point, with good improvement of local sagging.

Mazzucco et al.²¹ described the first series of neck and breast rejuvenation cases in 2009, in which³³ patients received the application of PLLA in the neck in the dilution of 10ml, with 3 patients also receiving it in the breast. The technique used was that of small 0.05ml bolus with a distance of 1 cm between the dermis and subcutaneous tissue. Peterson and Goldman³⁰ used a 16ml dilution, with retrograde technique in a fan shape, for rejuvenating breasts. Kaffler et al. presented a comparative study, conducted in the dermatology department of the Faculdade de Medicina do ABC (São Paulo, Brazil) in which 6 female patients underwent two PLLA treatments, with monthly intervals, in the inner part of the arms. In the right-hand side, the final dilution of the product was 20ml, and the technique used was the linear retrograde, with a final volume of 5ml. In the left-hand side, the final dilution of the product was 10ml, with point-to-point application, and a total applied volume of 2.5ml. In the follow-up, 6 patients reported less pain in the right-hand side (i.e. side with greater dilution), with none noticing differences in the final results. Five described important degrees of improvement in sagging, and 1 reported moderate improvement.³⁶

After each treatment, patients should be instructed to massage the area 5 times a day, for 5 minutes for 5 days^{4,8,12,13,24,27,30} using emollient creams to minimize friction during massage. This procedure can be extended up to one month.¹¹ Massage ensures the distribution of the product and prevents the formation of papules and nodules.⁵

The interval between sessions is typically four^{8,10,15} to eight³⁴ weeks, until the end of the treatment.¹¹ The total number of vials to be used is related to the surface area to be treated that requires volumization,^{11,13} in addition to the patient's age, degree of lipoatrophy and sagging. Patients with more severe lipoatrophy may need 2 bottles per session¹⁹ and up to 5 or more sessions to achieve the desired result, although most treatments require 1 bottle per session and 2 or 3 sessions.^{19,22} According to Lacombe,¹⁹ if the treatment is performed in the middle and lower third of the face, two vials are necessary. Some authors, like Goldman,⁸ wait for an interval of 12 weeks after the 3rd session, in order to evaluate whether there is a need for additional treatment.

In order to increase tissular volume, the initial treatment yields a base with a new fibrosis matrix.⁶ The final outcome will be achieved within a period varying from four to six months.¹⁹ Due to the volume of the product's reconstitution, the patient will leave the practice with the appearance of having in fact undergone a filling procedure, with the understanding that such improvement will disappear in a few days and he or she should then wait for production of collagen to start in six to eight weeks.

Once volumization has been achieved, results can be maintained for three years or more.¹⁹ According to Vlegaar,³² PLLA appears to be stable for 30 to 40 months²³ after treatment. Salles et al.,² showed good results for 36 months in 40% of ten treated patients. According to the publication of Faces,¹⁰ a prospective study of 290 HIV-seropositive patients undergoing

treatment with PLLA, after two years 79% of them had Grade I (almost normal) in the James' scale, independent of phototype, age, or gender. In a 5-year retrospective follow-up study, Rendon²⁰ suggests that the duration of the results is dependent on the patient's age, initial dermal thickness and bone structure prior to treatment, with patients under 55-years-old presenting a prolonged duration.

Adverse reactions related to the use of PLLA, such as echymoses, hematomas, edema, papules, nodules, and granulomas, mainly appear at the sites of injection of the product. The reported incidence of papules ranges from 31-44%¹⁰ in dilutions of 4ml or less; with higher rates—of around 13.9% or less—in dilutions greater than 5ml.^{29,30,34}

Papules and nodules are mostly only palpable and not visible, and dependent on the application technique. They are related to large volumes injected superficially^{37,38} or the non-interruption of the application before withdrawing the needle,²² with the application of little diluted product^{10,30,37,38} and use in areas with thin skin (such as the infraorbital,^{18,37} perioral,²⁰ and temporal regions), and areas of hypermobility,²³ in addition to cases where massage is not performed after the procedure.^{21,30} Intradermal injections should be avoided.³⁰ Sessions held at four to 6 week intervals³⁰ minimize the formation of nodules. Papules are usually transient and disappear spontaneously through the phenomenon of transepidermal elimination.²² In the Faces publication,¹⁰ 76.9% of papules and nodules were resolved spontaneously after two years. In the experience of Sherman, topical retinoids (0.025%–0.1% tretinoin) and superficial chemical peels (glycolic, lactic, mandelic, or salicylic acids) can help resolve or prevent the formation of papules.

It is important to differentiate papules, nodules, and granulomas after treatment with PLLA. A nodule may be visible or not, painful or not,⁹ hardened with a clear boundary between it and the surrounding tissue, with a size that does not change up until it is reabsorbed, treated, or removed.¹⁶ Typically, it only appears several weeks after injection, and¹⁶ represents a PLLA grouping.¹⁶ The coalescence of these particles can be broken with the fragmentation of the nodule and injection of saline solution (SS) using a Luer-Lok syringe, 1-3ml of 0.9% SS with 25G needle to hydrate and redistribute the particles, followed by aggressive massage, 16—all of which can be repeated weekly until improvement of the situation,^{16,21,22} which resolves in 80% of cases.² Non-visible and untreated nodules tend to remain stable for two, 8 three,³² or more years.

Although PLLA is an inert substance, it can still stimulate foreign body reaction.¹⁸ The function of these reactions is to isolate and prevent the migration of particles that cannot be readily removed by phagocytosis and enzymatic degradation.⁹

Granulomas can be characterized by particle aggregates of chronic inflammatory cells forming nodules, typically of a few millimeters in diameter. What distinguishes granulomas from other components of the inflammatory response is a collection of macrophages and epithelioid cells, usually surrounded by lymphocytes. In granulomas, macrophages are modified into giant multinucleated cells.⁹ Histologically, nodules consist of

fluid droplets or microparticles of various sizes that are: irregularly shaped;⁷ birefringent under polarized light;³⁹ surrounded by a foreign body in a reactive state;^{9,16} with macrophages and giant multinucleated cells^{7,18,37} and few inflammatory cells.¹⁷ Granulomas are delayed nodules, which appear several months after application, and which may be treated with intralesional corticosteroid of 0.02–0.04 ml triamcinolone.^{16,22} These applications can be repeated at intervals of 2 to 4 weeks. If not resolved, they can be removed surgically. Goldman, 8 who has treated more than 1,000 patients with PLLA, makes it a practice not to leave non-visible nodules to disappear spontaneously, since the application of intralesional corticosteroids may cause dissolution of perinodular fat, making them more evident. As an alternative, he opts for a surrounding application of hyaluronic acid to make them less evident. The reported incidence of granulomas related to the use of PLLA is low: 0.01–0.1% (Vleggaar described six granulomas in 3,000 treated patients).¹⁶

Treatment of granuloma can also be carried out with the use of corticosteroid therapy¹⁶ (orally with prednisone 60mg/day,⁴⁰ intralesionally with triamcinolone acetonide 40mg/ml every three weeks for a total of 1 to 10 applications,²⁸ or intramuscularly), minocycline^{9,28,40} as an anti-inflammatory, immunomodulator and with antigranulomatous properties.⁹ Another option is to use 5-fluorouracil^{9,40} (50mg/ml) isolated or combined with 1mg/ml triamcinolone acetonide or 7mg/ml betamethasone, which can reduce the skin atrophy rate.^{16,40} Another effective combination is 1/3 of 5-fluorouracil (1.6 ml), 1/3 of betamethasone (3.5 mg) and 1/3 lidocaine.¹⁶ Vleggaar has reported success with intralesional injections of 0.4 ml of 5-fluorouracil with 0.6 ml triamcinolone acetonide (10mg/ml), weekly for 4 weeks, in addition to oral corticosteroids of 100 mg minocycline daily for 8 weeks.¹⁶ In the beginning of the treatment, other authors use a combination of two antibiotics, such as second-generation cephalosporin and third-generation macrolide, for seven days.²⁸ Surgical excision is more difficult due to the absence of a clear boundary between the healthy tissue and tissue affected by the granulomatous reaction.^{16,28} In 2008, Goldman reported 4 cases of female patients who were all heavy smokers who had granulomas in the lip region and who had all been treated for 2 to 6 months with PLLA; each had subsequently undergone antibiotic therapy and intralesional corticosteroids—with one of them also undergoing drainage of multiple abscesses.⁴¹

In 2009, Alijotas-Reig et al.¹⁷ published a report on adverse effects in 10 patients treated with PLLA where the following had occurred 15 months after receiving the application of poly-L-lactic acid: 3 patients with inflammatory nodules, 1 with papules and nodules, 5 with nodules and facial edema, and 1 with inflammatory nodules on the face and with erythematous papules in the arms and legs (with a histological diagnosis of sarcoid reaction). In the last case, the patient had undergone an implantation of hyaluronic acid and methacrylate 36 months before the application of PLLA. The patient was treated with hydroxychloroquine, prednisone, and ibuprofen. Although the time elapsed between these two procedures and the appearance of adverse effects after PLLA had been long, the question of whether this granulomatous

reaction was caused by the interaction of the two fillers. In theory two or more different antigenic stimuli can increase the risk of abnormal immune response and produce immune-mediated adverse effects. In vitro, all bioimplants can cause a foreign-body reaction based on macrophage activation and induction of T-cells. Theoretically, the development of the collagen network coincides with the decrease in inflammatory reaction, however the so-called stable granulomas may evolve into a progressive granulomatous reaction after minor trauma or infections. In this clinical series, 2 of the patients who had nodules and edema had also been treated with permanent implants.

Other rare complications that need to be mentioned are: 1 case of amaurosis and one case of angioedema post-PLLA. The first refers to a 43-year-old HIV-seropositive man who received PLLA in the lateral nasal and periorbital regions, who had amaurosis caused by intra-arterial injection into the ophthalmic artery. This patient had undergone rhinoplasty, which can be an additional risk factor due to the impairment of the anastomoses of the ophthalmic artery.⁴² The other is the case of a 59-year-old woman without previous history of allergies, then using lisinopril, who underwent application of PLLA in the face and of hyaluronic acid with lidocaine in the lips. Two hours later, the patient developed significant edema in the lips and perioral region, having been hospitalized and properly treated. In that case, it was not clear whether the angioedema was caused by histamine release (either due to the trauma linked to the needle or to the intradermal injection of the product) in individuals who were predisposed and in use of angiotensin-converting enzyme inhibitors, or whether it was caused by the cutaneous filling substances. The authors attributed it to the PLLA, for the patient had previously undergone another application of hyaluronic acid without any complication.⁴³

There are several proposals of treatments adjuvant to PLLA aimed at obtaining harmonious aesthetic outcomes. If the treated area presents photodamage, the application of pulsed light or non-ablative fractional laser can be performed in the same session, provided it precedes that of the PLLA (in order to avoid contamination of the tips of the device with blood)⁸ without increasing the risk of adverse effects related to the association.¹² Lowe²³ suggests the association of other treatments, such as the application of hyaluronic acid and botulinum toxin, laser resurfacing, and radiofrequency. Others^{11,20} associate hyaluronic acid or calcium hydroxylapatite, provided the application procedures are performed with an interval of 30 days.

Several studies^{11,12,13} show high rates of patient satisfaction after treatment with PLLA. Vleggaar reported that 95.1% of patients were satisfied with the results, while Hanke et al. and Salles reported 89.5% and 60.0% patient satisfaction, respectively.¹¹

CONCLUSION

Poly-L-lactic acid is a safe and effective product for the volumization of the face, correction of unaesthetic scars, and for the treatment of sagging, with predictable and good aesthetic results, provided that it is properly prepared and used. ●

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