

Poly-L-lactic Acid for the Treatment of Trauma-Induced Facial Lipoatrophy and Asymmetry

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Poly-L-lactic acid (PLLA) is approved by the US Food and Drug Administration (FDA) for the treatment of human immunodeficiency virus (HIV)-associated lipoatrophy. Over the past several years, PLLA has been increasingly used as a treatment for lipoatrophy secondary to the natural process of aging. There have been no reports on the use of PLLA for trauma-induced facial lipoatrophy and asymmetry. In this article, we review the safety, effectiveness, treatment guidelines, mechanism of action, and quality-of-life (QOL) impact of PLLA. We present a patient with facial lipoatrophy and asymmetry secondary to injury from a motor vehicle accident that was effectively treated using PLLA. The future role of PLLA in the treatment of trauma-induced facial lipoatrophy and asymmetry, as well as other disorders, also is discussed.

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Poly-L-lactic acid (PLLA) was approved by the US Food and Drug Administration (FDA) in 2004 for human immunodeficiency virus (HIV)-associated lipoatrophy. Prior to its approval in the United States, it was extensively used

in Europe under a different brand name. In Europe, PLLA has been used since 1999 for the treatment of HIV-associated lipoatrophy as well as volume replacement in the correction of wrinkles and scars. PLLA is an immunologically inactive, synthetic, and biodegradable polymer derived from vegetables.¹ Its efficacy and safety have been demonstrated, as it has been used in suture material, medical devices, and maxillofacial implants.²

Injectable PLLA is freeze dried as 40 to 60 nm microspheres in a suspension of sodium carboxymethylcellulose and nonpyrogenic mannitol. This suspension allows for storage at room temperature up to 30°C for up to 2 years. Prior to injection, PLLA microspheres are diluted in a carrier solution of 4 to 6 mL of sterile water. When more global use is desired, dilutions of up to 6 to 8 mL have been used. A dilution time of at least 2 hours is needed to insure proper reconstitution. An additional 1 to 2 mL of lidocaine 1% with or without 1:100,000 epinephrine can be added to the suspension immediately prior to injection, providing further procedural anesthesia and hemostasis. Reconstituted PLLA is drawn into 3-mL sterile syringes and injected into the deep dermis using a minimum 26-gauge sterile needle with a length of 0.5 to 0.75 in, allowing for proper product flow. Although some injectors have used 25-gauge needles, we have consistent positive results using a 26-gauge needle. In our experience, the wider the opening size, the less control one has over the volume injected, and the wider opening size also adds to local trauma and bruising. The product feels natural under the skin and molding is not necessary with proper placement. It is important to massage the areas injected for a minimum of 5 minutes postprocedure and to have the patient continue to massage the areas

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Figure 1. A 64-year-old woman with facial lipoatrophy and asymmetry before (A) and 6 months after initial course of therapy with poly-L-lactic acid (B).

3 times daily for 5 days to allow for even distribution of product and to help prevent papule formation by encouraging incorporation of PLLA microspheres into dermal tissue.

Initial injection of product causes volume expansion, followed by subsequent resorption of carrier solution. Reversion to pretreatment volume generally occurs within 48 hours. PLLA microspheres undergo phagocytosis, are metabolized to crystals, and go through a foreign body reaction. The crystals act as a foundation for the formation of new collagen bundles by fibroblasts. Generally, 3 to 4 treatments administered 4 to 6 weeks apart over 4 to 6 months allow for substantial collagen production and the visual appearance of increased volume. In our experience, an increase in facial volume usually is noted several months into the course of therapy, with an average correction time of 2 to 3 years.

Over the past several years, PLLA has been increasingly used as a treatment for facial lipoatrophy secondary to the natural process of aging. The efficacy of PLLA for this aesthetic use has been documented.^{3,4} In reviewing the literature, there have been no reports on the use of PLLA for trauma-induced facial lipoatrophy and

asymmetry. The following case report discusses the use of PLLA in a patient with facial lipoatrophy and asymmetry secondary to injury from a motor vehicle accident.

Case Report

A 64-year-old woman presented in February 2005 for a cosmetic consultation. The patient was involved in a traumatic motor vehicle accident in 1967, resulting in extensive craniofacial damage and morbidity. The accident was a head-on collision and the patient's face hit the dashboard. There were multiple fractures of the right orbit, including loss of the eye and avulsion of the eyelid. The right mandible, as well as the frontal and occipital skull, had multiple fractures. The patient underwent intermittent hospitalizations for one year for facial reconstructive procedures, placement of an artificial eye, and treatment of other bodily injuries. In subsequent years, several other reconstructive procedures were attempted to reduce visible defects. The patient stated that her visible appearance after the accident resulted in years of clinical depression and embarrassment. The social and emotional implications of the patient's physical appearance



Figure 2. A 64-year-old woman with facial lipoatrophy and asymmetry 4 weeks after the first treatment with poly-L-lactic acid (A) and 6 months after initial course of therapy with poly-L-lactic acid (B).

made a considerably negative impact on her quality of life (QOL).

Treatment Regimen—Initial examination of the patient in February 2005 revealed bilateral facial lipoatrophy, with the right side of the face being more severely affected (Figure 1A). The temples, zygomatic arch, jawline, cheeks, and chin also were affected, displaying marked facial lipoatrophy. Severe lipoatrophy also was apparent overlying the left zygomatic arch. The facial bones appeared to be more anterosuperior on the right side, giving the face a lopsided appearance (Figures 1A and 2A). Clinical treatment options were discussed with the patient, including calcium hydroxylapatite, hyaluronic acid, and autologous fat transplantation. PLLA was chosen because of the patient's desire for volume replacement, longevity of correction, and lack of necessity for further surgical intervention.

The initial treatment with PLLA was performed a few days after the consultation. A total of 5 mL of reconstituted PLLA was placed into the deep dermis of the cheeks (2 mL), nasolabial folds (1 mL), zygomatic arches (1 mL), temples (0.5 mL), and chin (0.5 mL), with more focus on the right side than the left. A half-inch 26-gauge needle was used for placement of product with the linear threading and depot injection techniques.

The patient returned for evaluation and subsequent treatments with PLLA in March, May, and July 2005. The amount of PLLA injected at subsequent visits (March and May) was identical to the initial treatment. Two vials of PLLA were used for the last treatment; a total of 10 mL of product was placed, emphasizing the right face and including the right cheek and preauricular area (4 mL), left cheek (1 mL), zygomatic arches (1 mL), nasolabial folds (2 mL), temples (1 mL), and chin (1 mL). The patient also underwent permanent makeup in April 2005, including lip liner, eyeliner, and eyebrows. She received a total of 4 treatments at 4- to 6-week intervals. Clinical photographs were taken before and after each treatment, and areas where product had been placed were mapped using a facial diagram. A follow-up visit was conducted in August 2005 to evaluate the response to the course of therapy. The pretreatment and posttreatment photographs were evaluated and results were discussed with the patient.

Treatment Results—Figures 1B and 2B show the final results 6 months following the initial course of PLLA therapy. There was a dramatic improvement in volume overlying the bilateral zygomatic arches and cheeks. The severe lipoatrophy of the left zygomatic arch was filled in nicely and both sides were

nearly symmetric. There also was evident improvement in volume overlying the nasolabial folds, temples, and chin. The sunken periorbital region also had improved secondary to the expansion in volume overlying the zygomatic arches. Prior to the procedure, the face was lopsided because of the anterosuperior prominence of the underlying bones secondary to traumatic fractures. After treatment with PLLA, the face was more aesthetically pleasing, with more balance and harmony.

The most noticeable improvement was in the patient's emotional disposition. The dramatic improvement in the patient's physical appearance had given her increased confidence and a new outlook on life. The patient, who had been self-conscious for 40 years because of her appearance, enjoyed regular compliments from friends and family following treatment with PLLA.

Comment

The use of PLLA for the treatment of facial lipoatrophy secondary to HIV-associated lipotrophy has been increasing since it was approved by the FDA for use in the United States. The aesthetic use of PLLA off-label for the treatment of lipoatrophy secondary to the natural process of aging also has been increasing in recent years. Although PLLA has been approved by the FDA for HIV-associated lipoatrophy only, its off-label use for the treatment of facial lipoatrophy secondary to the natural process of aging has been increasing exponentially. The safety and efficacy of PLLA therapy in HIV-associated facial lipoatrophy has been proven by multiple studies.³⁻⁷ Several reports describing the safety and efficacy of PLLA in the natural process of aging have been published.⁸⁻¹⁰ There have been no reports in the literature on the use of PLLA for treatment of trauma-induced lipoatrophy and facial asymmetry for craniofacial defects.

The VEGA study (conducted in France) evaluated the efficacy, safety, and durability of facial injections with PLLA to treat HIV-associated lipoatrophy in 50 patients.³ The patients underwent 4 to 6 biweekly treatments within 2 years. An increase in dermal thickness was measured using ultrasonography. The results showed a mean increase in skin thickness of 6.8 mm at the 96-week end point. Additionally, QOL was measured using the visual analogue scale in 44 patients. QOL progressively increased between baseline and week 48.³

In England, the Chelsea and Westminster (C&W) study measured dermal thickness in 2 groups of patients with HIV and facial lipoatrophy after 3 injections of PLLA conducted at 2-week intervals within 24 weeks.¹¹ One group received 3 initial injections

at 0, 2, and 4 weeks of the study, and a second group received delayed injections at 12, 14, and 16 weeks. At 12 weeks, there was a statistically significant ($P < .001$) increase in dermal thickness in the first group. At the study end point, there was a mean increase of approximately 4 to 6 mm in dermal thickness in all patients, with no significant difference between the 2 groups. Improvement in QOL was demonstrated using the Hospital Anxiety and Depression Scale. All patients described a positive impact on QOL at weeks 12 and 24 of treatment.¹¹

In 2 US studies, the APEX 002 and Blue Pacific, the overall satisfaction in patients undergoing a 12-month trial of PLLA therapy was evaluated.^{11,12} Ninety-nine patients with HIV-associated facial lipoatrophy were enrolled in each study and underwent up to 6 injections of PLLA at 3- to 6-week intervals. The mean volume injected was 7.8 and 6.0 mL, respectively. Patient satisfaction was equivalent in both studies, reported as 4.7 out of a maximum of 5.0 at the end of the 12-month trial.^{11,12}

The most common adverse effect of PLLA is formation of asymptomatic dermal or subcutaneous papules and nodules.¹¹ In the VEGA and C&W studies, dermal nodules were reported in 52% (26/50) and 31% (9/29) of patients, respectively.^{3,11} This adverse reaction can be minimized by postinjection massage of the treated area.¹¹ Additional adverse effects reported in the VEGA and C&W studies included bruising, edema, discomfort, hematoma, inflammation, and erythema.^{3,11} A late-onset foreign body granulomatous reaction has been described as a possible complication of therapy with PLLA.^{13,14} The early lower dilutions also are believed to have a causal effect in the formation of papules. Our patient did not report any adverse effects from the course of PLLA therapy. The side-effect profile in this patient has been consistent with all of our patients since 2004. Dependent on the degree of lipoatrophy, we typically use 1 or 2 vials of PLLA per treatment session. The use of more than 2 vials per treatment session may increase the side-effect profile, though this observation has not been studied and depends on the degree of lipoatrophy. Overall, PLLA is well-tolerated, with virtually no serious adverse effects. The only contraindication to use of PLLA is hypersensitivity to any of the intrinsic or suspension components.¹¹ It also should be used with caution in patients that have received silicone or other permanent filler agents.

Conclusion

This case report demonstrates that PLLA can be used for correction of facial lipoatrophy and asymmetry secondary to traumatic injury. Our patient had dramatic

improvement in facial volume and symmetry. As seen in our patient, PLLA treatment can have a profound positive impact on QOL, which has been supported by both the VEGA and C&W studies.^{3,11} PLLA should be considered in the treatment of trauma-induced facial lipoatrophy and asymmetry. Additionally, PLLA may have a future role in the treatment of congenital abnormalities, as well as defects caused by surgical procedures. Compared with other therapeutic modalities, the use of PLLA in these disorders is promising because it is minimally invasive and requires little recovery time. More studies need to be done researching the application of PLLA and other filler materials in the treatment of other disorders. It is important to remember, with the recent FDA approval of new filler agents, the positive impact these agents can have on our patients' lives.

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