The Clinical Study of Poly-D, L-Lactic Acid (PDLLA) Biostimulator Injection for Improving Facial Rejuvenation Markers in Young Thai Individuals

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Received 23 April 2025 • Revised 2 June 2025 • Accepted 19 June 2025 • Published online 1 September 2025

Abstract:

Background: Aging is an inescapable and complex biological phenomenon that affects the skin, leading to changes such as wrinkles, sagging, pigmentation irregularities, and decreased elasticity. The latest trend in biostimulators has had a significant impact on facial rejuvenation, with poly-D, L-lactic acid (PDLLA) standing out. However, clinical trials on its long-term effects and safety remain limited, especially in Thailand.

Objective: The objective of this study was to investigate the effects of PDLLA injection in young Thai individuals for facial rejuvenation.

Materials and Method: In this quasi-experimental design, fifteen participants with mild to moderate facial aging signs enrolled at Mae Fah Luang University Hospital Asoke, Bangkok, Thailand. Each participant underwent subdermal PDLLA injections over a six-month period. Skin quality was evaluated at baseline and at 2, 4, and 6 months using validated instruments that measured eight facial rejuvenation parameters including sebum level, elasticity, skin hydration, transepidermal water loss (TEWL), spots, pores, wrinkles and texture. The study also evaluated the Global Aesthetic Improvement Scale (GAIS), patient satisfaction scores and any treatment-related side effects.

Results: All 15 participants showed significant improvement in elasticity, skin hydration, transepidermal water loss, pore size, and wrinkles from baseline to 6 months ($p < 0.001$). However, no significant differences were observed in sebum levels, spots, or texture. Mild skin erythema was observed in only one case (6.67%), which was spontaneously reversible over time.

Conclusion: Our study shows that PDLLA offers promising results for facial rejuvenation and can be an alternative for skin aging prevention, especially in young individuals, with no serious side effects when proper injection and reconstitution techniques are followed.

Keywords: Poly-D, L-lactic acid, Elasticity, TEWL, Hydration, Pore

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GMSMJ 2025; 5 (3): 159-168

Introduction

Facial rejuvenation treatments have gained significant attention in recent years, particularly among younger individuals seeking non-invasive solutions to maintain a youthful appearance. Beauty concerns related to aging, such as loss of facial volume and the appearance of fine lines, have become prevalent even among younger populations due to environmental factors, lifestyle choices, and genetics.[1] Thailand, like many countries globally, is experiencing a shift toward an aging population. According to national data, the proportion of individuals aged 60 and above in Thailand is 20 percent and is steadily increasing[2], leading to an increasing demand for preventive aesthetic treatments aimed at delaying or reversing the early signs of aging. Poly-D, L-lactic acid (PDLLA), a synthetic polymer derived from corn and potato starch[3-4], has emerged as a leading biostimulator in aesthetic medicine due to its ability to promote collagen synthesis through an inflammatory process, as proven by *in vitro* and *in vivo* studies.[5-7] PDLLA is biodegradable, with a study of PDLLA screws used in knee surgery showed complete resorption with intact surrounding tissue after 22 months.[8]

Although PDLLA has been widely studied and used in aging populations[7,9-10], there is limited research on its effectiveness in younger individuals, particularly in Thai populations. Younger individuals often seek preventative treatments that maintain or delay visible signs of aging, rather than reversing established signs. Understanding the impact of PDLLA injections on facial rejuvenation markers in young individuals is crucial for establishing its role in addressing the root causes of aging through early-stage aesthetic interventions. Therefore, this study aims to investigate the effects of PDLLA biostimulator injections on key facial rejuvenation markers, including sebum level, elasticity, skin hydration, transepidermal water loss (TEWL), spot, pore, wrinkle, and texture, in young Thai individuals. The outcomes will provide insights into the safety, efficacy, and long-term benefits of PDLLA as a preventive treatment, contributing valuable information to the growing field of aesthetic medicine.

Materials and Method

Study design and Participants

A quasi-experimental design was conducted for a before-and-after design from May 2024 to January 2025, recruiting 15 participants at Mae Fah Luang University Hospital Asoke, Bangkok, Thailand.

Sample size calculation

The sample size was calculated based on a study of Bohnert K, et al.[11] N4Studies Software, Version 1.4.0, was used to calculate the sample size. Estimated sample sizes were determined using a two-dependent means formula[12], based on a 5% α error, 80% power, and a 95% confidence level. The required number of patients for the study was calculated to be 15 after adjusting for a 20% dropout rate.

Method

The included participants were either male or female aged between 30 to 45 years with mild to moderate facial aging signs. We excluded individuals with poor medical conditions, active skin diseases, pregnancy or breastfeeding, and those with a history of biostimulator use. The study protocol was approved by the Ethics Committee on Human Research of Mae Fah Luang University (approval no. COA 97/2024). The scope of the work was explained to all participants and informed consent was obtained before participating in the study.

Materials

Study participants received injections of poly-D, L-lactic acid (PDLLA), commercially known as AestheFill (REGEN Biotech, Seoul, Korea), administered in two sessions spaced two months apart, as collagenesis typically reaches its peak around this time.[6] The Korean Food and Drug Administration granted initial approval for this product in 2014.[6] It also received approval from the Thai Food and Drug Administration (TFDA) under registration number 66-2-1-2-0004634. The product was supplied as a freeze-dried powder in vials, each containing 200 mg, composed of 154 mg of PDLLA and 46 mg of carboxymethyl cellulose (CMC). Prior to injection, 8 mL of sterile water was added to the PDLLA vial. Immediately before administration, an additional 2 mL of 2% lidocaine without adrenaline was incorporated, yielding a final dilution of 10 mL. The back-and-forth technique was utilized to ensure thorough mixing.[13] Local anesthesia (0.2 mL per site) was administered at the pre-hole, positioned along an imaginary line between the mid-preauricular and lateral canthus lines. Injections were delivered using a multilayer injection technique. A 23G blunt cannula was inserted at an angle of 30 to 40 degrees. A 23G cannula was chosen for its balance between flexibility and precision, minimizing tissue trauma and reducing the risk of bruising. Each injection line received 0.5 mL, with a total of five lines per side. Each participant received up to 2.5 mL of PDLLA per side, amounting to 5 mL per session.

Data collection

The assessments were conducted at specific time points (0 month, 2 months, 4 months, and 6 months). Demographic data, including age, gender, underlying disease, occupation, and personal history were collected. Data of the facial rejuvenation markers including the Sebum Level as measured by Sebumeter®[14], Elasticity as measured by Cutometer®[15], Skin Capacitance as measured by Corneometer®[16], Transepidermal Water Loss (TEWL) as measured by Tewameter®.[17]

Before each measurement, the Sebumeter® was zeroed by measuring the initial transparency of the tape without sebum present to ensure accuracy.[14] The Cutometer® was cleaned with a special brush and calibrated using a check cap per on-screen instructions.[15] The Corneometer® was calibrated *in vitro* using filter paper saturated with saline to simulate high hydration and a polyurethane film to represent low hydration, ensuring the device operated within validated measurement ranges.[16] The Tewameter® was calibrated using a check cap placed over the probe to create a sealed environment, allowing internal vapor concentration to be compared against skin measurements to detect and correct any drift.[17]

The first measurement site was identified at the intersection of the mid-pupil line and mid-tragus line, while the other four sites were positioned 1 cm above, below, left, and right of this point. The investigators performed each measurement five times on each side at every follow-up, totaling ten measurements per follow-up.

In addition, another four parameters of facial rejuvenation markers were assessed using the Visia-CR.[18] The participant was positioned in the machine, which automatically captured images and analyzed spots, pores, wrinkles, and texture, measured in arbitrary units (a.u.). Participants' satisfaction with the PDLLA injection was collected at the end of the study using a five-point Likert scale, while side effects were assessed using a side effect record form.

Statistical analysis

Data was analyzed using SPSS version 28.0 with *p*-value of less than 0.05 was considered statistically significant. The demographic data were presented as mean ± SD, while categorical data were expressed as frequency. The Shapiro-Wilk test was used to assess the normality of the data. Facial rejuvenation markers were analyzed using ANOVA with repeated measures for normally distributed data, while the Friedman test was applied when normality assumptions were violated. Participant satisfaction and side effects were reported as percentages.

Results

Demographic data of the 15 female participants (Table 1) showed an average age of 36.33 ± 3.85 years. Most had Fitzpatrick skin types 3 or 4 and no underlying conditions. None had allergies, took medications, or smoked, though some consumed alcohol. Participants came from various occupations, with housekeepers being the most common.

Throughout the 6-month study, notable changes in mean differences were observed. Significant improvements in Elasticity, Hydration, TEWL, Pore, and Wrinkle markers began at the 2-month mark and continued to increase over time, with the most significant difference noted from baseline to 6 months (-0.11 ± 0.02, $p < 0.001$). Conversely, Sebum levels, Spot, and Texture markers showed no significant changes, as outlined in Table 2.

At the end of the study, participants were asked to rate their overall satisfaction. The majority (93.3%) reported being extremely satisfied, while 6.67% were satisfied. The clinical changes were captured using VISIA-CR photographs in Figure 1. No major side effects occurred during the study. Throughout the study, no significant side effects were observed. The only reported issues were mild localized irritation, such as erythema (6.67%), which resolved on its own over time without any intervention.

Table 1 Demographic data of the 15 participants

Characteristics	Mean ± SD
Age (year)	36.33 ± 3.85
	Number of case
Sex	
Male	0
Female	15
Occupation	
Housekeeper	5
Therapist	3
Nurse	2
Office Employee	5
Business Owner	0
Unemployed	0
Fitzpatrick Skin Type	
Type 3	5
Type 4	10
Other	0
Underlying Disease	
None	15
Dyslipidemia	0
History of Food/Drug Allergy	0
Current Medication (Antibiotic, NSAIDs)	0
Current Smoker	0
Alcohol drinking	3

Table 2 The mean of facial rejuvenation markers at baseline, 2 months, 4 months, and 6 months (n = 15) with repeated measures ANOVA results

Markers	Baseline to 2 months (Mean Diff ± SD)	Baseline to 4 months (Mean Diff ± SD)	Baseline to 6 months (Mean Diff ± SD)	2 months to 4 months (Mean Diff ± SD)	2 months to 6 months (Mean Diff ± SD)	4 months to 6 months (Mean Diff ± SD)
Elasticity	-0.07 ± 0.02*	-0.16 ± 0.04**	-0.20 ± 0.03***	-0.09 ± 0.02***	-0.13 ± 0.02***	-0.04 ± 0.01***
Sebum level	0.01 ± 0.04	0.13 ± 0.08	-0.01 ± 0.26	0.11 ± 0.06	-0.03 ± 0.27	-0.14 ± 0.26
Hydration	-3.96 ± 0.98**	-8.76 ± 1.69***	-11.33 ± 1.65***	-4.80 ± 1.06***	-7.38 ± 1.11***	-2.58 ± 0.50***
TEWL	4.29 ± 1.31*	8.91 ± 1.14***	10.47 ± 1.17***	4.63 ± 0.73***	6.18 ± 0.79***	1.56 ± 0.27***
Spot	-0.08 ± 0.07	0.70 ± 0.11	0.26 ± 0.13	0.15 ± 0.07	0.33 ± 0.12	0.19 ± 0.11
Pore	3.21 ± 0.99*	8.43 ± 1.42***	9.90 ± 1.42***	5.21 ± 0.84***	6.69 ± 0.92***	1.47 ± 0.29***
Wrinkle	3.83 ± 1.06*	7.53 ± 1.18***	11.10 ± 1.43***	3.70 ± 0.99***	7.27 ± 1.35***	3.57 ± 0.73***
Texture	0.04 ± 0.06	0.26 ± 0.12	-0.22 ± 0.26	0.23 ± 0.11	-0.25 ± 0.26	-0.48 ± 0.28

Note Data were analyzed using Repeated measure ANOVA followed by Bonferroni post hoc tests, SD for (Standard Deviation), Mean diff for (Mean Difference), TEWL for (Transepidermal Water Loss), Values with different superscript symbols (*, **, ***) indicate statistical significance at $p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively.

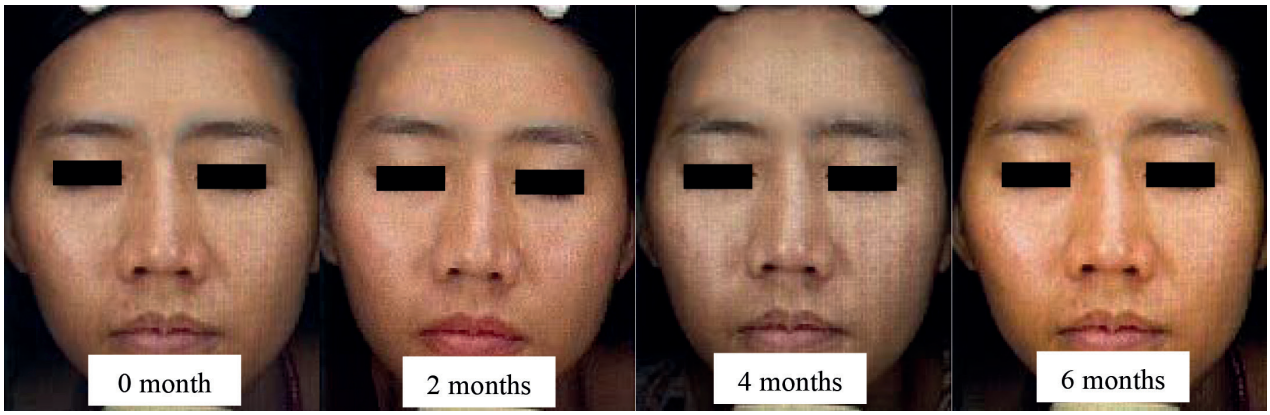

Figure 1 The comparison of VISIA-CR photographs of representative case at 0, 2, 4, and 6 months, respectively

Discussion

The present study aimed to evaluate the efficacy of poly-D, L-lactic acid (PDLLA) as a biostimulator for facial rejuvenation, focusing on various markers. The findings not only highlight the potential benefits of PDLLA in enhancing facial aesthetics but also contribute to the existing body of literature on biostimulator therapies.

In terms of effectiveness, the data indicated a statistically significant improvement in skin elasticity, hydration, TEWL, pore size, and wrinkles among participants receiving PDLLA treatment, starting from the second month. The early changes, particularly in hydration, may be attributed to the immediate filling effect post-injection. However, this effect diminishes after approximately two weeks, with subsequent improvements likely resulting from collagen synthesis.[5]

Our study could be applied to other biostimulator indications. For instance, Lin and Lin (2022) reported improved skin elasticity and hydration after a single-session PDLLA (AestheFill) injection for under-eye rejuvenation, using a 4 mL formulation (3 mL SWFI and 1 mL lidocaine) with 2 mL per side.[9] Given the delicate nature of the periorbital area, adapting our midface injection and dilution technique—such as using a 23G cannula for controlled, precise subdermal deposition—could further optimize outcomes while minimizing risks in periorbital treatments.

Likewise, a recent study by Seo et al. (2024) highlighted the use of PDLLA (Juvelook) for skin rejuvenation with a mesotherapy injector equipped with 32G 9-pin needles. The formulation, comprising hyaluronic acid (HA), lidocaine, and saline, was administered over three sessions in a study involving 16 participants and demonstrated promising results.[10] Given PDLLA's particle size (30–60 μm), the use of a 23G cannula, as in our study, provides advantages such as smoother delivery, reduced clogging, and controlled subdermal deposition, while also minimizing trauma, lowering vascular injury risk, and enhancing patient comfort. The selection of a 23G cannula is the reason why our study reported no bruising or serious side effects and achieved consistent clinical outcomes.

In terms of safety, Ianhez et al. (2024) reported complications from collagen biostimulators, with poly-L-lactic acid (PLLA) accounting for 69.1% of 55 cases, primarily nodules (89.1%), often persisting despite treatment.[19] PDLLA offers a safer alternative to PLLA, a similar chemical isomer. Bohnert et al. (2019) evaluated PLLA in three treatment sessions spaced four weeks

apart, requiring post-injection massage to prevent nodules.[11] Despite its efficacy, this additional step was necessary. In contrast, our study used PDLLA with a 23G cannula in only two sessions, achieving significant improvements in skin elasticity, hydration, and TEWL without massage. PDLLA may offer a safer alternative due to its smaller particle size, uniform degradation, and reduced nodule risk. PDLLA's smoother tissue integration eliminates the need for post-injection massage, unlike PLLA. Additionally, using a 23G cannula, as in our study, enhances safety by ensuring controlled placement and minimizing vascular injury. These differences underscore PDLLA's advantages, including a lower risk of nodules, fewer sessions, and controlled deposition, making it a promising option for facial biostimulation in young-aged individuals.

Our study introduces an innovative approach, highlighting the ideal candidates for PDLLA injection. These include the young-aged group with poor skin quality, such as loose skin, dry skin, large pore size, and fine wrinkles, particularly in the middle face area. Although PDLLA is safer than PLLA, there is a case report by Choi Min et al. (2024) of granulomas in the infraorbital area. A 58-year-old woman developed granulomas after her third PDLLA injection, which were unresponsive to TCA and light therapy, requiring surgery.[20] This emphasizes the importance of careful injection technique, especially in thin-skinned areas like the infraorbital region. Proper injection technique, including precise placement and appropriate dosage, is crucial to minimizing risks, as demonstrated in our study.

While the results of this study are promising, certain limitations should be acknowledged. This study's limited sample size and lack of participant or evaluator blinding may introduce potential bias and limit the generalizability of the findings. Although PDLLA injections have proven effective in facial rejuvenation, the study did not assess PDLLA's impact in combination with other procedures or on other body parts, where skin structure, thickness, and tissue response to substances may vary significantly. Future studies should explore PDLLA's impact on various skin types and demographics, as well as its combination with other procedures like laser treatments or microneedling. Expanding research to areas such as the neck, décolletage, and hands could provide further insights into PDLLA's efficacy and safety across different anatomical sites, optimizing clinical applications.

Conclusion

This study demonstrated that Poly-D, L-lactic acid (PDLLA) significantly improves facial rejuvenation markers, including skin elasticity, hydration, TEWL, pore appearance, and wrinkles over 6 months. Notable improvements were seen starting at 2 months, with continued progress after the second injection. PDLLA offers a safe alternative for skin aging prevention in young individuals, with no serious side effects when proper techniques are followed.

Acknowledgements

The authors would also like to express their sincere gratitude to the staffs at Mae Fah Luang University Hospital Asoke, Bangkok, Thailand, for their invaluable support with data collection.

Conflict of interest

The authors declare no conflicts of interest.

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