A Randomized, Split-Body, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Poly-L-lactic Acid for the Treatment of Upper Knee Skin Laxity

Ramya Kollipara, MD,* Elika Hoss, MD,† Monica Boen, MD,‡ Marwan Alhaddad, MD,§ and Sabrina G. Fabi, MD‡‖

BACKGROUND Skin laxity of the upper knee and lower thigh is a common complaint among patients.

OBJECTIVE This is a randomized, double-blinded, split-body, placebo-controlled study to evaluate the safety and efficacy of poly-L-lactic acid (PLLA) for treatment of upper knee skin laxity.

MATERIALS AND METHODS Twenty female subjects between the ages of 30 and 65 years with upper knee laxity were enrolled. The patients were randomized to receive 3 treatments of PLLA in 1 knee, whereas the other knee received 3 treatments of bacteriostatic water.

RESULTS Statistically significant improvement as rated on the physician global aesthetic improvement scale was seen at Day 56 after final treatment in the active knee when compared with the placebo knee. This improvement was sustained at Day 84 and Day 168 after final treatment visits. No statistically significant difference was seen between the active and placebo knees on the subject global aesthetic score or the subject satisfaction scale.

CONCLUSION Based on our study, PLLA may be a safe and effective modality in addressing upper knee skin laxity. Larger studies with longer follow-up times and a validated knee laxity scale are needed to further determine if and how much improvement can be achieved.

Funded by a grant from Galderma Laboratories LP. Medication was provided by Galderma Laboratories LP for the study. The authors have indicated no significant interest with commercial supporters.

Skin laxity of the upper knee and anterior thigh is a common complaint among patients. Safe and effective treatment options for upper knee laxity are scarce. Microfocused ultrasound with visualization has recently been shown to be effective for reducing skin laxity and crepiness of the knee but requires capital equipment. Microfocused ultrasound has shown to induce lifting and tightening by thermocoagulation of old collagen and stimulation of new collagen production.[1]

Because poly-L-lactic acid (PLLA; Sculptra Aesthethic; Galderma Laboratories, Fort Worth, TX) stimulates neocollagenesis, it is possible it may be beneficial in the treatment of lax skin of the knee. Poly-L-lactic acid is an injectable implant containing microparticles of PLLA, carboxymethylcellulose, and nonpyrogenic mannitol. It is currently approved by the FDA for the correction of shallow to deep nasolabial fold contour deficiencies and other facial wrinkles in immune-competent patients and for facial lipoatrophy in patients with HIV.[2] Poly-L-lactic acid microspheres

Westlake Dermatology & Cosmetic Surgery, Dallas, Texas; †Department of Dermatology, Mayo Clinic, Scottsdale, Arizona; ‡Cosmetic Laser Dermatology, San Diego, California; §Slocum-Dickinson Medical Group, New Hartford, New York; ‖University of California, San Diego, San Diego, California

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.dermatologicsurgery.org).

ISSN: 1076-0512 • Dermatol Surg 2020;00:1–5 • DOI: 10.1097/DSS.0000000000002685

stimulate neocollagenesis from fibroblasts, leading to volume correction. The PLLA microspheres themselves are gradually degraded and do not directly contribute to the final result. Three to 4 sessions every 4 to 6 weeks are needed to achieve optimal correction, which can last 18 to 25 months.[2–5] Most providers use PLLA to correct panfacial volume loss.[2,3]

Because PLLA stimulates neocollagenesis, it is possible it may also be beneficial in the treatment of lax skin of the knee. In this study, the efficacy, safety, and patient satisfaction of the treatment of knee skin laxity and crepiness with PLLA will be evaluated.

Materials and Methods

Study Design

This is a randomized, double-blinded, split-body, placebo-controlled study. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in approval by the institutional review board. Twenty female subjects between the ages of 30 and 65 years with symmetric, bilateral, mild to severe upper knee laxity on the upper knee laxity/crepiness grading scale (see **Supplemental Digital Content 1**, Figure S1, http://links.lww.com/DSS/A474) were enrolled. Subjects must have had a stable body weight for at least 6 months before study entry. Subjects were excluded if they had undergone any skin tightening treatments in the past 12 months, ever received biostimulatory/filler injections, or undergone nonablative laser treatments in the past 3 months in the treatment area. They were also excluded if they had a history of hypertrophic or keloidal scarring.

Active and Placebo Treatments

Each subject's knees were randomized to receive 3 treatments of PLLA 4 weeks apart in 1 knee, whereas the other knee received 3 treatments of bacteriostatic water and served as the control. The active side received 1 vial of PLLA diluted with 14 mL of bacteriostatic water and 2 mL of 1% plain lidocaine. The control side received 16 mL of bacteriostatic water. The treatment area was limited to the skin of the anterior upper knee. Injections were not placed lower than the superior border of the patella. The area treated was 10 cm in height (superior–inferior plane) and 10 cm in width (medial–lateral plane). The active and placebo product was injected with a 25 gauge, 1 ½ inch needle using a retrograde fanning technique. After the treatment session, patients massaged both knees for 5 minutes, 5 times per day, for 5 days.

Evaluation of Efficacy, Safety, and Satisfaction

Primary endpoints included the blinded investigator laxity/crepiness grading scale, the Physician Global Aesthetic Improvement Scale (PGAIS) by a blinded evaluator, and the blinded evaluator identification of the treated knee. The blinded investigator laxity/crepiness grading scale was performed at postfinal treatment days 28, 84, and 168. The PGAIS (see **Supplemental Digital Content 2**, Figure S2, http://links.lww.com/DSS/A475) was performed after treatment 3 and postfinal treatment days 28, 84, and 168. The blinded evaluator (by a different evaluator who did not perform the treatments) identification of the treated knee was performed after all subjects had completed the study.

Secondary endpoints included the Subject Global Aesthetic Improvement Scale (SGAIS) and the subject satisfaction questionnaire. Both these assessments were completed after treatment 3 and postfinal treatment days 28, 84, and 168. The treating physician also evaluated for side effects (erythema, edema, contour abnormality, and nodules) after every treatment and at postfinal treatment days 28, 84, and 168.

Photographic Documentation

Before each treatment and at the postfinal treatment days 28, 84, and 168 visits, standard 2D photographs were taken, capturing 3 views: anterior, right oblique (45°) and left oblique (45°). Vectra 3-D photography was also performed at these visits. The subjects were standing during all photographs.

Statistical Analysis

Statistical evaluation was performed with Microsoft Excel 2013. The 2-tailed Student *t*-test was used to determine the difference in means between groups. All data are represented as mean ± SD.

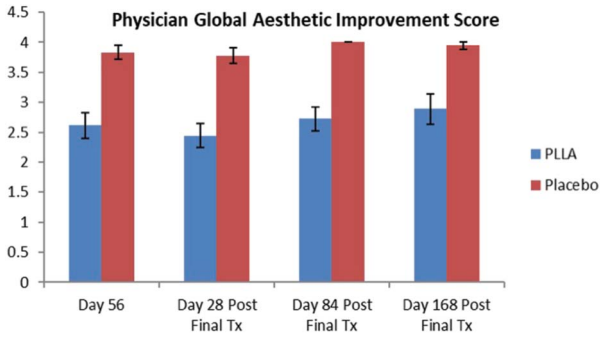

Figure 1. Physician Global Aesthetic Improvement Scale scores at Day 28, Day 84, and Day 168 after final treatment. All *p* values were <0.05. PLLA, poly-L-lactic acid.

Results

Subject Demographics

Twenty subjects were enrolled in the study. The mean subject age was 56.2 years (range 48.2–65.5 years of age). Eighteen patients completed the study, and 2 patients were lost to follow-up.

Efficacy

Statistically significant improvement as rated on the PGAIS was seen at Day 28 after final treatment ($p < 0.05$) in the active knee when compared with the placebo knee. This improvement was sustained at the Day 84 ($p < 0.05$) and Day 168 ($p < 0.05$) after final treatment visits (Figure 1). At Day 168 after final treatment, the mean PGAIS was 2.89 (1 = very much improved, 2 = much improved, 3 = improved, 4 = no change, and 5 = worse) in the active knee versus 3.94 in the placebo knee. At Day 84 after final treatment, 16 of 18 patients (89%) and 0 of 18 patients were noted to have improvement in their active and placebo knees, respectively. Of these 16 active knees with improvement, 2 were noted to be "very much improved," 3 were noted to be "much improved," and 11 were noted to be "improved." At Day 168 after final treatment, 12 of 18 (67%) patients and 1 of 18 (6%) patients were noted to have improvement in their active and placebo knees, respectively. A representative set of images can be seen in Figures 2.

No statistically significant difference in the blinded investigator laxity/crepiness scale was detected between the active and placebo knees at the days 56, 84, and 168 after final treatment visits (Figure 3). No statistically significant difference was seen between the active and placebo knees on the subject global aesthetic score or the subject satisfaction scale (Figures 4 and 5).

Blinded investigator assessments at the end of the study involved comparison of pretreatment and Day 168 after final treatment photographs. The blinded investigator was able to identify the post-treatment photograph in 5 of 18 patients and the active knee in 7 of 18 patients.

Safety and Tolerability

Poly-L-lactic acid treatments were well tolerated without any significant adverse events. Physician assessments of erythema, edema, contour irregularity, and nodules revealed no statistically significant difference between the active and placebo groups. There were no cases of edema, contour irregularity, or nodules in either the active or placebo knees. Mild erythema was noted in both the active and placebo knees in 6 of the patients at the Day 56 after the final treatment visit and had resolved in both knees at the Day 84 after the final treatment visit.

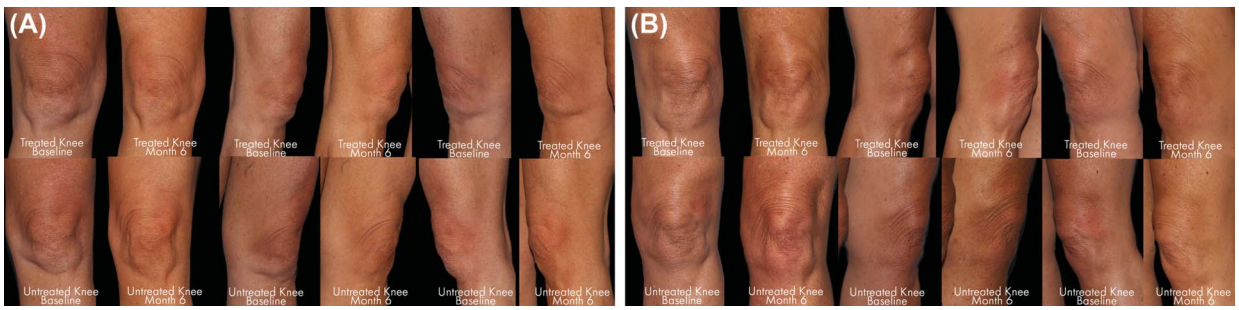

Figure 2. Patients (A and B): Treated (top) and untreated knee (bottom) at baseline and 6 months after final treatment from different angles.

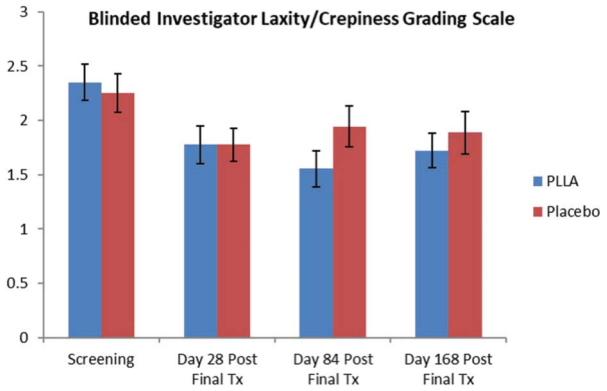

Figure 3. Blinded investigator laxity/crepiness scale at Day 28, Day 84, and Day 168 after final treatment. PLLA, poly-L-lactic acid.

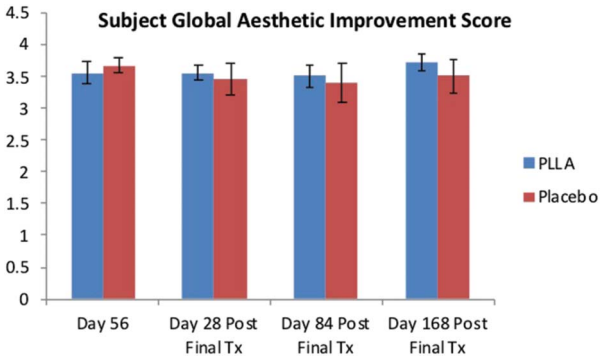

Figure 4. Subject Global Aesthetic Improvement Scale scores at Day 56 (56 days after first PLLA treatment) and Day 28, Day 84, and day 168 after final PLLA treatment. PLLA, poly-L-lactic acid.

Discussion

Given the rise of off-face skin tightening in the last decade, upper knee laxity has become a common concern among patients. Liposuction does not address laxity, and surgical removal of excess skin ("thigh lift") is an invasive procedure which does not adequately address knee laxity, and results in scars and possible adverse events. Resurfacing is also not an option given the paucity of sebaceous glands in this cosmetic unit.

Over the last decade, off the face application of PLLA has become more popular, and it has been used for chest wrinkles, buttock augmentation, and for crepiness of the arms.[6–9] This is the first study to assess the efficacy and safety of PLLA in the treatment of upper knee laxity. Based on our study, PLLA seems to be a safe and effective modality in addressing upper knee skin laxity. Significant improvement in the PGAIS was noted at Day 28 after final treatment, and this improvement was sustained at 84 and 168 days after final treatment. Specifically, 89% of subjects versus 0% of subjects were noted to have improvement in their active and placebo knees, respectively, at the Day 84 after the final treatment visit. Investigators continued to note a difference at the Day 168 after the final treatment visit as 67% (12 of 18) of subjects were noted to have improvement in the active knee versus only 6% (1 of 18) had improvement in the placebo knee. Poly-L-lactic acid treatments were also well tolerated without any incidence of nodules.

No statistically significant improvement was seen in the blinded investigator laxity/crepiness scales. This scale is not validated and therefore may not have been as sensitive to consistently and reliably capture improvement in skin quality and tightening. In addition, there were statistically significant changes in the SGAIS or subject satisfaction scores between the active and placebo knees. Lack of statistically significant outcomes in these measures may be due to the limited follow-up period of 6 months. Recent research has demonstrated that PLLA enhances skin quality in a time-dependent manner and that significant improvement in skin quality (specifically radiance, pore size, pigmentation, and smoothness) may not be seen until 12 months after the final treatment.[10] Thus as the follow-up period in this study was only 6 months, further improvement in laxity that may have occurred at 12 months was not captured.

Figure 5. Subject satisfaction scale scores at Day 168 after final treatment. PLLA, poly-L-lactic acid.

The limitations of this study include its small sample size, limited follow-up period of 6 months, and that it was conducted at a single center. A larger sample size may have allowed for clearer conclusions to be drawn regarding efficacy. Furthermore, a larger sample size would have allowed for detection of more subtle changes in the outcome measures. Finally, using a validated skin quality scale may have helped to detect nuanced changes in skin quality.

Poly-L-lactic acid may be an effective and safe non-invasive modality for treating laxity and improving the appearance of the upper knee. As microfocused ultrasound has also been shown to improve upper knee laxity, PLLA may be combined with microfocused ultrasound to enhance the improvement in upper knee laxity.[1] Combination laser/light treatments and injectables have become increasingly popular in the last decade because of the synergistic potential when certain treatments are paired together. Given the inconsistent results in this study, further studies with a larger sample size, longer follow-up period, a validated knee laxity scale, and combination therapy with microfocused ultrasound therapy can delineate the optimal therapeutic regimen to treat upper knee laxity.

References

1. Gold MH1, Sensing W, Biron J. Use of micro-focused ultrasound with visualization to lift and tighten lax knee skin. J Cosmet Laser 2014;16:225–9.
2. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf3/P030050S002c.pdf. Accessed August 19, 2016.
3. Narins RS, Baumann L, Brandt FS, Fagien S, et al. A randomized study of the efficacy and safety of injectable poly-L-lactic acid versus human-based collagen implant in the treatment of nasolabial fold wrinkles. J Am Acad Dermatol 2010;62:448–62.
4. Vleggaar D. Facial volumetric correction with injectable poly-L-lactic acid. Dermatol Surg 2005;31:1511–7.
5. Woerie B, Hanke CW, Sattler G. Poly-L-lactic acid: a temporary filler for soft tissue augmentation. J Drugs Dermatol 2004;3:385–9.
6. Lin MJ, Dubin DP, Khorsani H. Poly-L-lactic acid for minimally invasive gluteal augmentation. Dermatol Surg 2020;46:386–94.
7. Jabbar A, Arruda S, Sadick N. Off face usage of poly-L-lactic acid for body rejuvenation. J Drugs Dermatol 2017;16:489–94.
8. Mazzurco R, Sadick NS. The use of poly-L-lactic acid in the gluteal area. Dermatol Surg 2016;42:441–3.
9. Sadick NS, Arruda S. The use of poly-L-lactic acid in the abdominal area. Dermatol Surg 2017;43:313–5.
10. Bohnert K, Dorizas A, Lorenc P, Sadick NS. Randomized, controlled, multicentered, double-blinded investigation of injectable poly-L-lactic acid for improving skin quality. Dermatol Surg 2019;45:718–24.

Address correspondence and reprint requests to: Ramya Kollipara, MD, Westlake Dermatology & Cosmetic Surgery, 7515 Greenville Avenue, Suite 1030, Dallas, TX 75231, or e-mail: drkollipara@westlakedermatology.com