The Efficacy of Polynucleotide Derived from Salmon DNA for the Treatment of Striae Distensae: A Pilot Study

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Abstract

Striae distensae, known as stretch marks, are harmless skin lesions that significantly impacts the aesthetic appearance, leading to considerable concern among those affected. Although fractional CO2 lasers are a prevalent treatment option, there is a risk that employing higher laser energy might increase the likelihood of post-inflammatory hyperpigmentation. Therefore, this study aims to investigate the effectiveness of polynucleotide treatments on striae distensae through a 20-week intraindividual clinical trial involving ten volunteers who have had stretch marks for over 12 months. Throughout each session, the study protocol involved the administration of 1 milliliter of polynucleotide (PN) treatment to a predefined area of the abdomen, measuring 8 centimeters by 8 centimeters, for each participant. This procedure was conducted during the initial visit and subsequently repeated in the 4th and 8th weeks of the study. Baseline evaluations, along with assessments at weeks 4, 8, 12, and 20 post-treatments, utilized digital photography and Antera 3D imaging to quantify changes in volume, roughness, width, and melanin content and to apply the Manchester scar scale. Following a 20-week treatment period, polynucleotide injections resulted in a significant reduction in the volume, roughness, and width of striae compared to the baseline. Additionally, there was a significant decrease in the Manchester scar scale scores by the twentieth week compared to the initial measurements. In conclusion, polynucleotide injections have shown promising results in enhancing striae without serious side effects. However, further extensive research is imperative to thoroughly ascertain its effectiveness and any potential adverse effects.

Keywords**:** *Polynucleotide, Striae Distensae, Salmon-DNA, Skin Rejuvenation*

1. Introduction

Striae distensae (SD) are widespread atrophic skin scars that can adversely impact mental health. While the pathogenesis of SD is unclear, but its development is believed to be associated with alterations in essential extracellular matrix components, such as fibrillin, elastin, and collagen, whichplay a crucial role in maintaining therile in skin's tension resistance and elasticity. In SD-affected skin, there isi a significant increase in glycosaminoglycan levels and a marked decrease in fibrillin fibers near the dermal-epidermal junction. Additionally, there are alterationsalterations in the alignment of elastin and fibrillin fibers within the deeper layers of the dermis (Watson et al., 1998). .

Although numerous treatments for Striae distensae have been proposed, effectively managing SD remains a considerable challenge, as there is no universally accepted "gold standard" treatment established (Seirafianpour et al., 2021).

Several investigations have examined the potential of olydeoxyribonucleotide (PDRN) and Polynucleotides (PN) in tissue repair, wound healing, angiogenesis, and anti-inflammatory properties, revealing their efficacy in both in vitro and in vivo studies. Injecting highly purified DNA polynucleotides from trout gonads into the dermis has been demonstrated to stimulate the growth and vitality of human skin fibroblasts, as well as aid in the restructuring of the skin's matrix. This technique results in the rejuvenation

of vital skin components like collagen, elastin fibrils, and glycosaminoglycans, indicating its potential for enhancing skin regeneration ((Colangelo et al., 2021). The administration of PN and PDRN injections has been established for approximately two decades in numerous countries across various medical contexts. These applications encompass enhancing venous ulcers in the lower limbs, addressing retracting hypertrophic scars characterized by significant skin thinning in the malleolar area, managing knee osteoarthritis, and undertaking aesthetic procedures such as rejuvenating treatments for conditions like crow's feet, nasolabial folds, and surgical scars, among others. In a study involving five Korean women, a sequence of four long-chain PN filler injections was administered at two-week intervals for skin rejuvenation. The findings revealed significant improvements in pore size and skin thickness (Park, Seok, Rho, Kim, & Kim, 2016). Moreover, in studies concentrating on patients with post-thyroidectomy scars, the supplementary application of polynucleotide alongside conventional fractional laser treatments has been observed to substantially enhance wound healing and diminish post-operative scarring subsequent to thyroidectomy (Kim et al., 2018). Prior research has indicated that all patients encountered temporary post-treatment edema, erythema, and scaling, which spontaneously resolved within a week. No severe adverse events were reported, and there were no documented instances of anaphylaxis associated with the use of PDRN and PN.

Drawing from the aforementioned data, this study aims to investigate the potential application of polynucleotide injections in the abdominal area to address striae distensae. This proposition stems from the known ability of polynucleotide to stimulate collagen and elastin production. Thus, it is hypothesized that polynucleotide injections may also ameliorate skin atrophy, concluding striae distensae. Consequently, polynucleotide injections could emerge as a promising alternative for managing striae distensae, offering effectiveness while potentially minimizing adverse effects.

2. Objectives

To evaluate the efficacy of intradermal polynucleotide derived from salmon DNA in the treatment of striae distensae.

3. Materials and Methods

The study was conducted as a pilot study, intraindividual trial at the Dermatology Department of Benchakitti Park Hospital, Thailand, from June to December 2023. Approval for the study protocol was granted by the Human Research Ethics Committee of Thammasat University.

3.1 Patient selection

The study will involve 10 volunteers aged between 20 and 65 who have had striae distensae on the abdomen for longer than 12 months. Participants were excluded from the study if they met any of the following conditions:

1. Pregnancy or lactation
2. Local skin infection in the treated area
3. Individuals who had undergone treatments such as laser therapy, radiofrequency (RF) treatments, dermabrasion, microdermabrasion, or chemical peels within six months prior to the study.
4. Participants with a history of keloidal tendency, bleeding tendency, platelet disorder, psoriasis, vasculitis, autoimmune disease, or using anticoagulation medicine
5. Participants who applied topical corticosteroids, retinoid, vitamin C, or vitamin E within 2 weeks

3.2 Study methods

Polynucleotide derived from salmon DNA has been officially registered as a medical device pursuant to Section 17 of the Medical Device Act 2008 in Thailand by the PharmaResearch company. All studies concerning PN injection have consistently revealed no instances of anaphylaxis or any other serious adverse events.

For the study, a specific abdominal area of Striae distensae, measuring 8 centimeters by 8 centimeters (64 square centimeters), was chosen for treatment. This specific area was selected to align with the dimensions of the Antera 3D camera utilized in the study. At each session—initially, and then at 4 and 8 weeks—1 milliliter of polynucleotide was injected into this delineated area. Follow-up evaluations were conducted at the 12th and 20th weeks to monitor the treatment's progress and effects.

3.3 Assessments

Digital photography and Antera 3D imaging were conducted at baseline, 4 weeks, 8 weeks, 12 weeks, and 20 weeks after treatment to assess volume, roughness, width, and melanin.

Assessments were performed by a dermatologist using the Manchester Scar Scale at 0- and 20-week follow-up. The evaluation includes Color (Perfect = 1, Slight mismatch = 2, Obvious mismatch = 3, Gross mismatch = 4), Finish (Matte = 1, Shiny = 2), Contour (Flush with surrounding skin = 1, Slightly raised or indented = 2, Hypertrophic = 3, Keloid = 4), Distortion (None = 1, Mild = 2, Moderate = 3, Severe = 4) and Texture (Normal = 1, Just palpable = 2, Firm = 3, Hard = 4)

After each treatment, the skin's response, including any bruising, swelling, hematoma, and erythema, was closely monitored in the treated areas. Additionally, any potential adverse effects related to the treatment were observed and documented during each follow-up visit.

3.4 Statistical analysis

The data analysis was performed using IBM SPSS Statistics Version 26. Quantitative data related to the population were expressed using means and standard deviations (SD).

The study utilized the Generalized Estimating Equation (GEE) model to statistically analyze changes in volume, roughness, width, and melanin of striae as measured by Antera 3D. Evaluations occurred at weeks 0, 4, 8, 12, and 20, with a P-value under 0.05 indicating significant findings.

4. Results and Discussion

4.1 Results

4.1.1 Demographic data

A total of 10 female participants were enrolled in the study, and all of them completed the entire research protocol. The average age of the participants was 42.30 ±13.37 years, ranging from 22 to 63 years. (Table 1).

Table 1 Baseline demographic characteristics of participants

	n = 10
Females, n(%)	10 (100%)
Age (years), mean ± SD	42.30 ± 13.37 [22-63]

4.1.2 Volume of Striae distensae

During the study period of receiving Polynucleotide injection, the volume of striae distensae (mm^3) exhibited a steady decrease from 2.54±1.35 to 1.97±1.00, 1.69±0.98, 1.66±0.80 and 1.37±0.69 after the

fourth, eighth, twelfth and twentieth week of follow-up, respectively (see Table 2 and Figure 1). There was a statistically significant reduction in volume at the fourth, eighth, twelfth, and twentieth weeks of follow-up.

Table 2 Mean change of volume of striae distensae from baseline to different points of time

Mean change of volume from baseline (week 0)	Mean ± SD.	Mean change (95%CI)	p-value
Week 0	2.54 ± 1.35	Reference	
Week 4	1.97 ± 1.00	-0.57 (-1.04, -0.10)	0.018*
Week 8	1.69 ± 0.98	-0.85 (-1.32, -0.38)	<0.001*
Week 12	1.66 ± 0.80	-0.88 (-1.35, -0.40)	<0.001*
Week 20	1.37 ± 0.69	-1.17 (-1.64, -0.69)	<0.001*

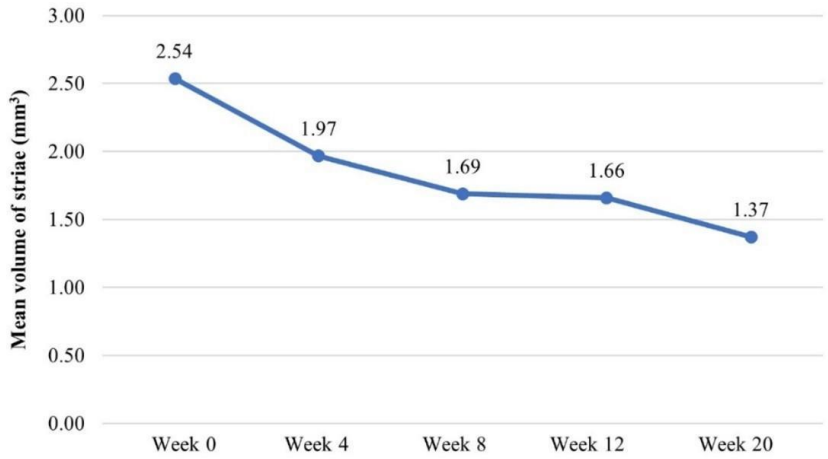

Figure 1 Comparison of mean volume of striae in different points of time

4.1.3 Roughness of Striae distensae

The roughness of striae distensae exhibited a gradual decline from baseline of 47.45±14.77 to 44.89±14.23 and 39.68±11.22 after the fourth and eighth weeks of follow-up, respectively. It slightly increased to 43.27±11.88 at the twelfth week. However, at the final follow-up appointment, the decline finally reached 38.50±8.65 (refer to Table 3 and Figure 2). Statistically significant decreases in roughness were observed at the eighth and twentieth follow-up weeks. However, the lack of significance at the twelfth week may be attributed to various factors. One possibility is that there could have been individual variations in response to treatment among participants, resulting in fluctuations in the observed results. Additionally, environmental factors might have influenced outcomes at various time points. Moreover, the study's small sample size could have constrained its statistical power to detect significant differences at certain intervals.

Table 3 Mean change of roughness from baseline to different points of time

Mean change of roughness from baseline (week 0)	Mean ± SD.	Mean change (95%CI)	p-value
Week 0	47.45 ± 14.77	Reference	
Week 4	44.89 ± 14.23	-2.56 (-9.16, 4.05)	0.449
Week 8	39.68 ± 11.22	-7.77 (-14.37, -1.16)	0.021*

Week 12	43.27 ± 11.88	-4.18 (-10.78, 2.43)	0.215
Week 20	38.50 ± 8.65	-8.94 (-15.55, -2.34)	0.008*

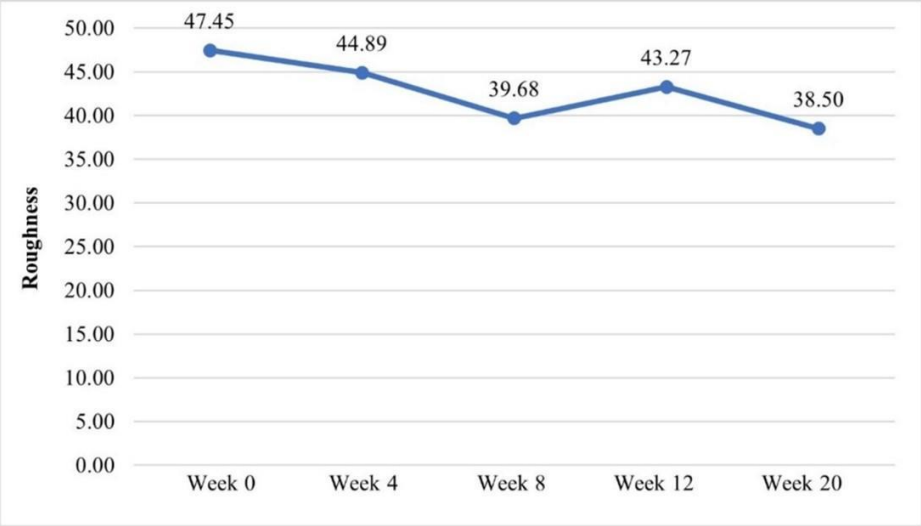

Figure 2 Comparison of mean roughness of striae in different points of time

4.1.4 Width of Striae distensae

The width of striae distensae (mm) showed an initial reduction from baseline of 2.24±0.54 to 2.10±0.37 at the fourth week of follow-up. There was a slight increase to 2.17±0.39 at the eighth week, followed by a consistent decrease to 2.05±0.41 and 2.01±0.45 after the twelfth and twentieth weeks of follow-up, respectively, with statistically significant reductions observed at the twelfth and twentieth weeks (see Table 4 and Figure 3).

Mean change of width from baseline (week 0)	Mean ± SD.	Mean change (95%CI)	p-value
Week 0	2.24 ± 0.54	Reference	
Week 4	2.10 ± 0.37	-0.14 (-0.32, 0.03)	0.115
Week 8	2.17 ± 0.39	-0.07 (-0.25, 0.10)	0.415
Week 12	2.05 ± 0.41	-0.19 (-0.36, -0.01)	0.039*
Week 20	2.01 ± 0.45	-0.23 (-0.40, -0.05)	0.012*

Table 4 Mean change of width from baseline to different points of time

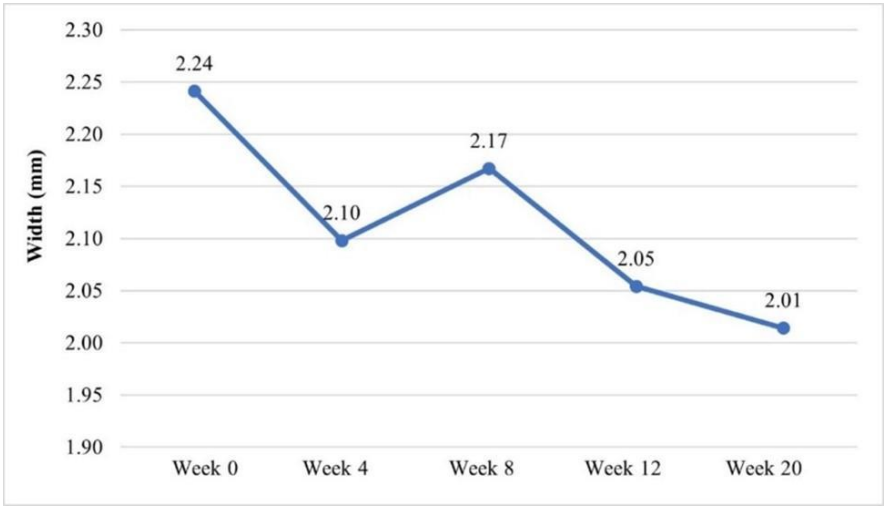

Figure 3 Comparison of mean width of striae in different points of time

4.1.5 Melanin of striae distensae

The melanin levels in striae distensae at the fourth, eighth, twelfth, and twenty weeks of follow-up did not significantly differ from the baseline values of 0.30 and 0.31. No statistically significant change in melanin levels was observed at any follow-up week (refer to Table 5 and Figure 4).

Table 5 Mean change of melanin from baseline to different points of time

Mean change of melanin from baseline (week 0)	Mean ± SD.	Mean change (95%CI)	p-value
Week 0	0.30 ± 0.09	Reference	
Week 4	0.31 ± 0.08	0.01 (-0.01, 0.02)	0.259
Week 8	0.31 ± 0.07	0.00 (-0.01, 0.02)	0.737
Week 12	0.31 ± 0.06	0.01 (0.00, 0.02)	0.189
Week 20	0.31 ± 0.07	0.01 (-0.01, 0.02)	0.272

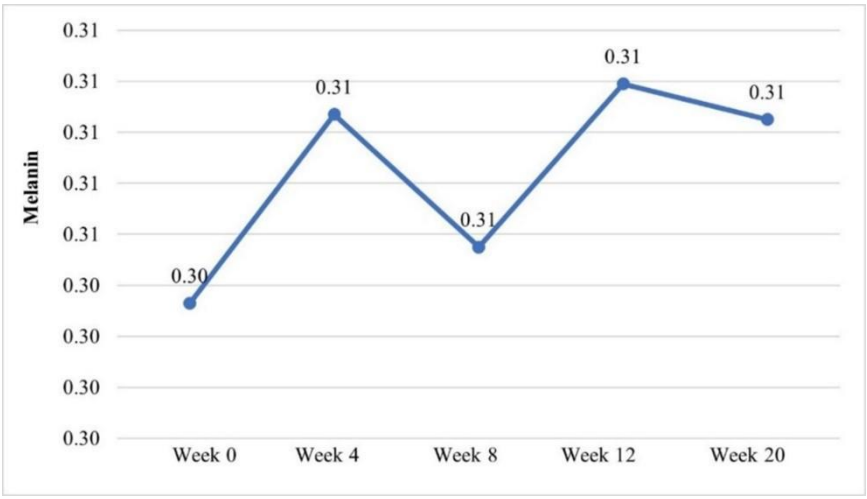

Figure 4 Comparison of mean melanin of striae in different points of time

4.1.6 Manchester scar scale

The Manchester scar scale for striae distensae decreased from a baseline of 12.00±1.56 to 7.40±0.97 after the twentieth week of follow-up (refer to Table 6 and Figure 5). A statistically significant decrease in scale was observed.

Table 6 Mean change of Manchester scar scale of baseline and twentieth week follow-up

Mean change of Manchester scar scale from baseline (week 0)	Mean ± SD.	Mean change (95%CI)	p-value
Week 0	12.00 ± 1.56	Reference	1
Week 20	7.40 ± 0.97	-4.60 (-5.78, -3.42)	<0.001*

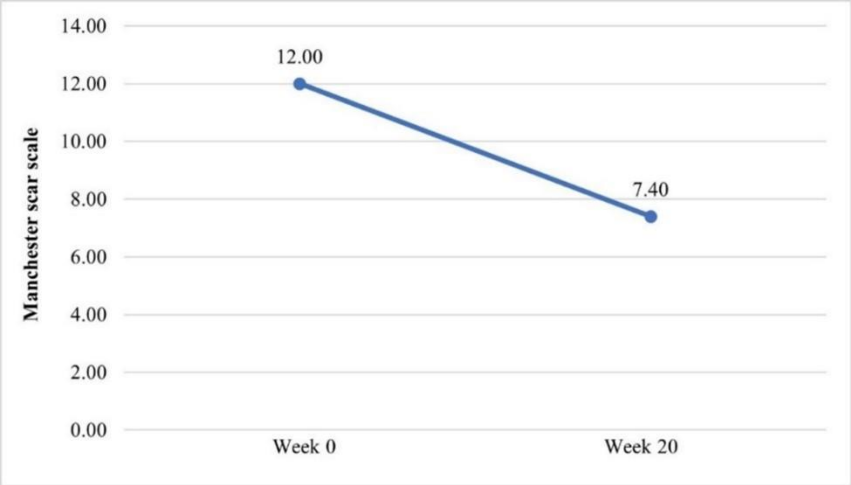

Figure 5 Comparison of Manchester scar scale of striae in different points of time

4.2 Discussion

Stretch marks, medically termed striae distensae, present a challenging treatment dilemma and can have a profound impact on mental well-being, despite not posing significant physical health risks. While numerous treatments exist, achieving effective results remains elusive. Fractional CO2 Lasers are among the favored options for their ability to regenerate collagen and elastin fibers. However, the use of higher laser energies carries a risk of post-inflammatory hyperpigmentation (PIH), potentially persisting for up to a year, underscoring the crucial importance of cautious treatment application (Seirafianpour et al., 2021).

Polynucleotides (PN), obtained from salmon germ cells and comprising both DNA and RNA, are instrumental in enhancing fibroblast survival and proliferation, along with boosting the production of collagens such as Collagen 1a1 and Collagen 3a1, essential for effective wound healing (Bainbridge, 2013). Treatment with polynucleotides has been demonstrated to facilitate the repair of various skin components, including collagen, elastin fibers, and glycosaminoglycans, contributing to skin rejuvenation and repair (Colangelo et al., 2021).

There is a pilot study (Matera, Dodici, & Raichi, 2020) involving three participants that explored the use of PN combined with laser therapy to improve striae distensae on the abdomen. The study demonstrated promising results in the combined treatment group compared to both PN monotherapy and the untreated group. The combination approach resulted in an average reduction of approximately 30% in the depth of stretch marks, particularly showcasing significant improvements in the depth of medium-wrinkled and thin striae when polynucleotide infiltrations were administered alongside laser treatments.

This study, a pilot study, intraindividual trial, compared the effectiveness of polynucleotide injections for treating striae distensae before and after treatment over a 20-week follow-up period involving ten volunteers. It evaluated changes in volume, roughness, width, and melanin using an Antera 3D camera at baseline and during follow-ups at the 4th, 8th, 12th, and 20th week. Additionally, the Manchester scar scale was assessed at the start and the end of the study.

In our study, participants who received polynucleotide injections exhibited a consistent decrease in the volume of striae distensae. Measurements indicated significant reductions from baseline up to the twentieth week, underscoring the treatment's effectiveness over time. Furthermore, the roughness of striae distensae demonstrated a gradual decrease from the initial assessment, with particularly noteworthy reductions noted at the eighth and twentieth weeks. These findings highlight the treatment's effectiveness in enhancing skin texture. Moreover, Polynucleotide (PN) injections demonstrated a consistent decrease in the width of striae distensae, with significant reductions observed at both the 12th and 20th weeks of the study. Throughout the study, melanin levels remained relatively stable with no significant changes from baseline to the 20th week, while the Manchester scar scale demonstrated a significant improvement at the 20th week, indicating a reduction in both the severity and appearance of striae distensae. The study's limitations include a small sample size and the use of a specific dosage of PN, which may limit the generalizability of the findings to other anatomical areas affected by striae. A more extended follow-up period is necessary for comprehensive outcome comparisons. Importantly, no severe adverse events were reported throughout the study.

5. Conclusion

The study findings suggest that polynucleotide injections effectively improve striae distensae by reducing volume and width while enhancing skin smoothness, with no serious side effects reported. Future research should expand on these findings with larger participant groups to further validate the treatment's efficacy and safety. Comparisons with other treatments, like fractional CO2 laser therapy, are also suggested for a comprehensive assessment of therapeutic options.

6. Acknowledgements

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