

Comparison of the effectiveness of microneedling with topical insulin versus saline (as a placebo) in the treatment of striae Alba using Antera 3D camera. Controlled left-right comparative study

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Abstract

Background

Striae Alba is caused by overstretching of the skin's dermis with permanent structural alteration of collagen fibers and scarring of the dermis. Microneedling stimulates a cascade of growth factors by multiple cutaneous injuries, which stimulates the migration, and proliferation of fibroblasts with the synthesis of new collagen. Insulin is of interest in the field of wound repair and can help in restoring the integrity of damaged skin.

Objectives

Evaluation of the clinical response, efficacy, safety, and adverse effect of combined microneedling with topical insulin compared to microneedling alone (with saline as a placebo) in treating stria alba.

Subjects and methods:

In this controlled left/right comparative study, microneedling with saline (as a placebo) was done on the right side of the abdomen, while the left half of the microneedling was done using topical insulin. For each patient; we did four sessions with 1 month in-between. We evaluated the treatment outcome using photographic documentation and a 3D Antera camera and measured the decrease in the indentation index.

Results

A significant decrease was found in the stria-alba indentation index after treatment in both the insulin sides and placebo sides; the insulin side being superior. There was no statistical significant difference between them as regards the side effects like erythema and hyperpigmentation.

Conclusion

Microneedling with topical insulin is an effective and safe method for treating patients with striae alba.

Introduction

Striae distensae is a common dermatologic problem that involves the lower portion of the back, buttocks, upper arms, breasts, and inguinal areas and is sometimes accompanied by itching¹. Striae distensae usually occur in many physiological conditions such as weight gain, pregnancy, elevated corticosteroid hormone level, and the genetic predisposition also plays a role²⁻⁴.

Various treatment modalities are available such as topical therapeutic agents used for the treatment of SD. Tretinoin and retinoic acid are the most effective in several studies. Other agents like hyaluronic acid are effective in Stria alba as they increase collagen production^{5,6}. PRP has a good result for its role in collagen remodeling, and acceleration of wound healing⁷. Laser resurfacing is safe and effective, with greater efficacy in striae alba⁸.

Skin micro-needling is also called needle dermabrasion. It is a simple, effective, safe, and cheap procedure for skin rejuvenation and facial scars by increasing collagen synthesis, also it is used nowadays as a trans-epidermal drug delivery system for vaccines⁹. This new collagen formation takes at least 6 weeks and the final result may need 3 months¹⁰.

Insulin is well known for its wound healing capacity as in dressings for diabetic foot ulcers, also it modifies the inflammation process, accelerating epithelialization, and neovascularization¹¹⁻¹³.

The application of topical insulin is done by spraying, in creams, dressings for wounds, and local injections.¹².

Materials and Methods

Twenty Female patients were recruited for this controlled comparative study suffering from striae alba on both sides of the abdomen. The diagnosis was made via clinical diagnosis of dermatological findings.

Approval of the research ethics committee (FWA 000017585), and all the patients were informed about the procedure steps and side effects, and written informed consent was obtained from each patient.

Inclusion Criteria:

1. Age ranged from 18-50 years old.
2. Female patients with Striae Alba on both sides.
3. No concurrent topical or systemic treatment for striae Alba during the last 3 months.
4. Patients with Fitzpatrick skin type up to V

Exclusion Criteria:

1. Pregnancy and lactation.
2. Patients with striae rubra.
3. Patients suffering from concomitant connective tissue disorder, infectious, inflammatory, or autoimmune cutaneous or systemic disease.
4. Patients with any problems with wound healing, or used any therapy for their striae albae in the past 6 months.
5. Dermatological disorders with isomorphic reaction (Koebner phenomenon).

6. Deranged blood sugar levels

Methods: *All patients were subjected to the following:*

1. **Full history taking:** including name, age, pregnancy status, lactation, and detailed history for the striae alba.
2. **Photographic documentation:** by using a 12 M.P. optically stabilized dual camera (S.M- N.95, Vietnam), and wide angle (F/1.70IS). Standard digital photographs were taken from 3 views of the abdomen at the first visit before treatment, then every four weeks of treatment
3. **Antera camera:** Antera camera was used to measure the indentation index of stria on both sides of the abdomen, before treatment and four weeks after the last session (week 16). It was also used to detect the melanin level before and after treatment.

Procedure:

- a. Microneedling with saline (as a placebo) was done to the Rt. side of the abdomen, while the left side micro-needling was done with topical insulin.
 - b. A session every 4 weeks (weeks 0, 4, 8 & 12) was done for every patient. Topical anesthetic cream (Pridocaine, GLOBAL NAPI PHARMACEUTICALS - EGYPT) was applied for 30 minutes with plastic film occlusion. Then we removed the cream and the area was disinfected with 70% alcohol. On each side, 3 passes of micro-needling were done on the striae only.
1. Lesions on both sides of the abdomen were treated with micro-needling using *dermapen (Dr pen ultima A6) using 36 needles with 2 mm depth*. A session was performed every 4 weeks for 4 sessions. Dermapen was passed in various directions with moderate pressure.
 2. *After completing micro-needling, 1-2 ml of topical insulin was applied on the left side of the abdomen (human act rapid 100IU/ml solution)*, while 1-2 ml of normal saline (as placebo) was applied on the other half of the abdomen.
 3. The abdomen was covered by saran wrap for 3-4 hours.
 4. Patients were advised to use topical antibiotics (fusidic acid ointment) two times per day for one week after treatment, followed by body moisturizer for 3 weeks.
 5. We instructed them to avoid sunlight exposure for the following 2 weeks.

4. Evaluation of the treatment outcome: CLINICAL ASSESSMENT.

The percentage of reduction in the width of striae was calculated in every patient 4 months after the first treatment session, and the results were rated as:

1 – 25%= slight improvement.

26 – 50%= mild improvement.

51 – 75%= moderate improvement.

76 – 99%= excellent improvement.

Photographic evaluation and Antera camera evaluation:

The indentation index of striae was measured and compared in all patients, baseline, and 4 weeks after the last session (week 16) using 3D Antera camera analysis software.

Assessment of side effects:

Clinical examination by using the Antera camera for post-procedural hyperpigmentation, and erythema. Also, pain, edema, infection, and hypoglycemia were assessed.

Data management and Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23.

Continuous numerical variables were presented as mean and striae distansae and paired differences were compared using the paired-samples Student t-test. The Stuart-Maxwell test of marginal homogeneity was used to compare paired ordinal data on multiple levels. The p value was considered significant as the following: More than 0.05 = Non significant, less than 0.05= significant, and if less than 0.01= highly significant.

Results

Twenty female patients with striae alba completed this split-abdomen prospective comparative study. Their mean age was 29.75 ± 4.58 y (21 to 38 Y). 10 patients had Fitzpatrick skin type III, while the other ten patients skin type IV.

Before treatment, the indentation index of the right (Rt) side was 17.75 ± 5.31 and of the left (Lt) side was 18.12 ± 5.20 . The melanin concentration on the right side was 0.57 ± 0.08 and on the left side 0.57 ± 0.08 . Both sides were matched, as there was no statistical significant difference between the Lt. side (insulin gr.) and the Rt. Side (saline gr.) as regards indentation index ($P= 0.825$) as well as melanin

Table (1): Comparison between indentation index and melanin concentration before and after treatment on the Rt. side (microneedling with saline):

Saline (Placebo) group		Before treatment	After treatment	Difference	Test v.	P. val.	Signific.
Indentation index	Mean \pm S.D.	17.75 \pm 5.31	14.77 \pm 3.69	-2.98 \pm 3.56	3.743	0.001	HS
	Ran.	11.45 – 30.85	9.04 – 22.79	-9.84 – 5.25			
Melanin	Mean \pm S.D.	0.57 \pm 0.08	0.67 \pm 0.08	0.10 \pm 0.07	7.059	<0.001	HS
	Ran.	0.36 – 0.72	0.48 – 0.78	-0.01 – 0.29			

•: Paired t-test

A decrease in the depth of the striae and an increase in pigmentation after treatment with micro-needling and saline (placebo). A high statistical significant difference was found as regards indentation index and melanin content before and after treatment with a P-value 0.001(for indentation index) and P-value <0.001 for melanin as shown in Table (1).

Table (2): Comparison between indentation index, and melanin concentration before and after treatment in Lt. side (microneedling with insulin):

Insulin group		Before treatment	After treatment	Difference	Test v.	P. – val.	Signif.
Indentation index	Mean \pm S.D.	18.12 \pm 5.20	11.44 \pm 2.62	-6.68 \pm 4.64	-6.432	0.000	HS
	Ran.	10.47 – 27.66	9 – 19.747	-15.846 – 1.596			
Melanin	Mean \pm S.D.	0.57 \pm 0.08	0.67 \pm 0.08	0.10 \pm 0.05	10.046	<0.001	H.S.
	Ran.	0.34 – 0.69	0.48 – 0.80	0 – 0.2			

•: Paired t-test

Similarly, on the insulin-micro-needle-treated side (Lt Side), the depth of SA decreased and pigmentation increased. A high statistical significant difference as regards indentation index and melanin content before and after treatment (P= 0.0001 and P<0.001) was found for indentation index and melanin content respectively as shown in Table (2).

Comparing the insulin-treated side with the placebo side:

The depth of the SA was less on the insulin-treated side compared with the placebo (saline) side. There was a better improvement of the indentation index on the left side compared to the right side (P val. = 0.012).

Table (3): Comparison between Lt side (insulin side) and Rt side (saline side) regarding indentation index difference and melanin difference after treatment by the Antera camera:

Difference		Saline (placebo) group	Insulin group	Test val.	P. val.	Signif.
Indention index	Mean ± S.D.	-2.98 ±3.56	-6.68 ± 4.64	-2.516	0.012	S
	Ran.	-9.84 –5.25	-15.846 – 1.596			
Melanin	M. ± S.D.	0.10 ±0.07	0.10 ±0.05	-0.068	0.946	N.S
	Ran.	-0.01 –0.29	0 –0.2			

‡: Mann Whitney test

However, no statistical significant difference was found between them as regards post-procedural hyperpigmentation (P=0.946) as shown in Table (3).

Side effects: All the patients presented with erythema on the first day of the procedure, only 4 patients had erythema more than 1 day. No other side effects happened.

Clinical improvement:

On comparing the clinical improvement in both sides of the abdomen regarding improvement, a significant difference was found between the 2 sides with p-value = 0.021, as shown in Table (4), figure (1), and figure (2).

Table (4): Comparison between Lt side (insulin side) and Rt side (micro-needling with saline) regarding clinical improvement after treatment

Improvement	Saline (placebo) gr. N. = 20	Insulin gr. N. = 20	Test val.	P. –val.	Signif.
Med.(IQR)	3(2 - 4)	4(3 - 4)	-2.945‡	0.003	H.S.
Ran.	2 – 4	2 – 4			
Mild	9 (45.0%)	2 (10.0%)	7.766*	0.021	S
Moderate	5 (25.0%)	4 (20.0%)			
excellent	6 (30.0%)	14 (70.0%)			

‡: Mann Whitney test; *: Chi-square test

In the right side of the abdomen (Placebo): 6 patients showed excellent improvement (30.0 %), 5 patients showed moderate improvement (25.0%) and 9 patients showed mild improvement (45.0 %).

In the left side of the abdomen (Insulin): 14 patients showed excellent improvement (70.0 %), 4 patients showed moderate improvement (20.0 %) and 2 patients showed mild improvement (10%)

Discussion

Striae distansae (SD) or stretch marks are very common, asymptomatic, skin condition frequently seen among females, despite several advances, no fully effective treatment has emerged ^{14,15}.

Insulin is responsible for the metabolism of glucose and fats, and the activation of tumor necrosis factor (T.N.F.-) and nuclear factor kappa beta (N.F.k-β) respectively which inactivates the inflammatory signaling. Although, insulin can activate the protein kinase B (A.k.t) pathway and increase the expression of endothelial nitric oxide synthase (e-NOS), matrix metalloproteinase (M.M.P.s), mechanistic target of rapamycin (m-TOR) leading to angiogenesis. Also, it reduces the expression of N.F.k.β.P50/ P65 through the M.E.K., and E.R.K. pathways. ¹⁶.

We aimed in our study to evaluate the effect of combining topical insulin with microneedling on the improvement of striae and microneedling alone. In 20 females, the left side was subjected to microneedling with topical insulin, while microneedling was used with saline on the right side. We did 4 microneedling sessions every 4 weeks; finally follow-up was 4 weeks after the last session.

In this study, we chose our patient's ages ranging from 18 to 40 years (M.= 34), as this age is the most common age of occurrence of striae ¹⁷.

We assessed our patients using an Antera 3D camera, also we chose an indention index, and this parameter is similar to the roughness definition, used to determine the texture of the skin. The difference lies in the fact that only the negative vertical deviations of the surface from its ideal form are considered, leading to a value of roughness that is solely dependent on indentations in the skin and not on protrusions, also we choose the indention index to assess large surface area rather than a single stria.

There was a statistical significant decrease in the indention index and the depth appearance of striae on both sides from baseline till follow-up.

On the placebo side, the indention index showed marked improvement, this improvement could be related to the action of microneedling which is mediated by macrophages that release numerous growth factors which stimulate the migration and proliferation of fibroblasts which stimulates the keratinocytes to rebuild the basement membrane by production of laminin and collagen types IV and VII ¹⁸.

The improvement on the insulin-treated side was significantly better than the saline-treated side as noted clinically and objectively by the Antera camera. Fourteen patients on the insulin side had excellent improvement in comparison to six on the placebo side. This results shows that the combining topical insulin with the microneedling yields better results than microneedling alone. This could be related to the action of topical insulin, which increases synthesis and maturation of collagen fibers, chiefly type III which occurs in a basket weave-like organization (normal skin), rather than a crisscross manner (scar) ¹⁹.

Insulin acts on the skin and increases re-epithelialization by stimulating keratinocytes to proliferate and migrate to the affected site, also it increases wound tensile strength, and stimulates fibroblasts to produce local Insulin-Like growth Factor; which stimulates cell growth and enhances wound healing. ¹³.

Our results are comparable to Pawar and Singh who studied the insulin effect on acne scars, they used PRP with microneedling in one half of the face and insulin was used in the other (**insulin act rapid 40 IU**). The insulin-treated side showed 45% total improvement and the PRP-treated side showed 26% total improvement in post-acne scars ¹⁹.

Patients were satisfied with both procedures. More patients were satisfied with the insulin-treated side and would recommend it to others, however, this result did not reach statistical significance.

In the current study, we did not encounter any serious adverse effects. Only mild pain, transient erythema, edema, and post-inflammatory hyperpigmentation on both sides. Most importantly, there was no clinical evidence of hypoglycemia, which was our primary concern, as assessed by measuring the blood sugar level before and after the session.

In conclusion, adding topical insulin to microneedling is a safe, effective, affordable, and promising drug for treating striae alba.

Declarations

Ethical statement: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the research ethics committee of faculty of medicine, Ain Shams University of a No. (FWA 000017585).

Informed consent was obtained from all individual participants included in the study after informing her about the steps of the procedure and the expected effects or possible complications. The authors affirm that human research participants provided informed consent for publication of the images in the Figure (2).

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Conflict of Interest: The authors declare that they have no conflict of interest.

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Author Contribution

M. A. and S. I. putted the design of the study and reviewed the final results of the paper.S.I. and A.R. collected the patients, examined the patients before, after 6 weeks and after 12 weeks with the 3D Antera camera and wrote these results.A.R. and A.E. followed up with the patients and analyzed the date and wrote the paper.

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Figures

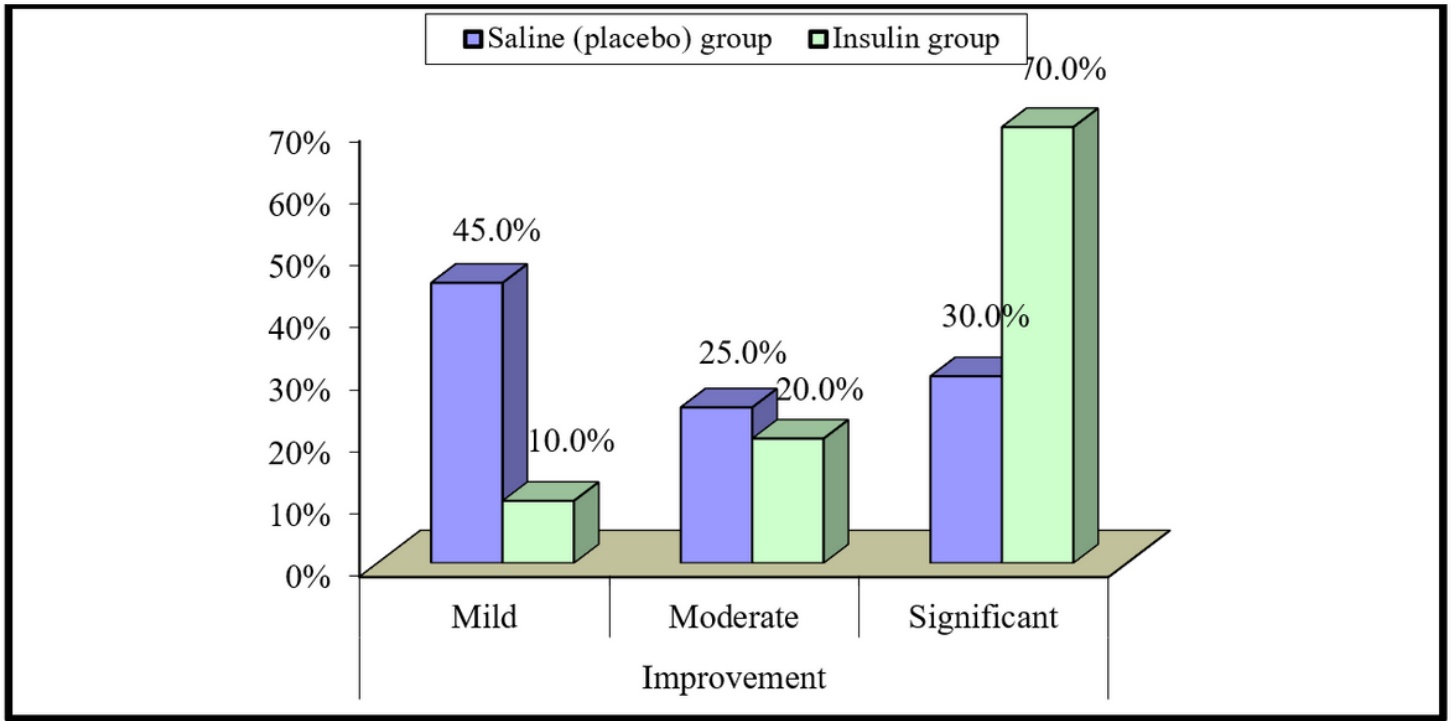


Figure 1

Comparison between microneedling with topical insulin and microneedling with saline regarding clinical improvement after treatment with p-value = 0.021.

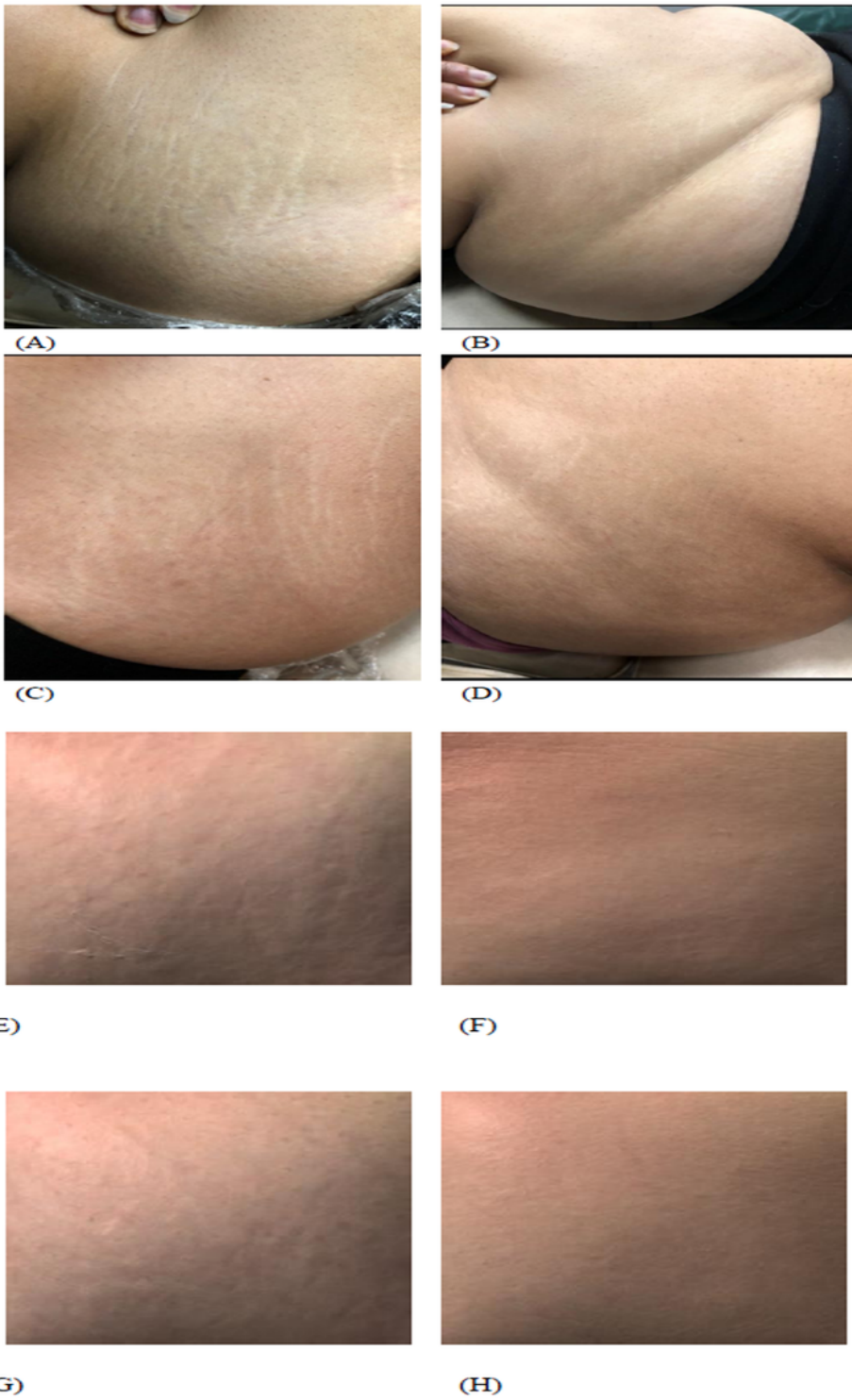


Figure 2

Showing the changes in the Stria alba with the camera and the Antera camera:

A: Rt. side before treatment, B: Rt. side after 3m. of follow-up showing excellent improvement, C: Lt. side before treatment, D: Lt. side after 3m. of follow-up showing excellent improvement. E: Rt. side before

treatment, F: Rt. side after 3m. of follow-up showing a marked decrease in indentation index, G: Lt. side before treatment, H: Lt. side after 3m. of follow-up showing a marked decrease in indentation index.