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Efficacy of tissue fibroplasia mesotherapy in reducing signs of skin ageing

Skuteczność mezoterapii z wykorzystaniem mechanizmu fibroplazji tkankowej w redukcji oznak starzenia się skóry

ABSTRACT

Tissue fibroplasia, the combination of a biorevitalising mechanism with a biostimulant in a single mesotherapy preparation, is a relatively new group of injectable products.

The study aimed to evaluate the effect of preparation with hyaluronic acid and sodium succinate on skin improvement in women with dry skin and clear signs of ageing.

It showed a statistically significant decrease in skin echogenicity compared to the original state, an increase in skin thickness and a shallowing of individual wrinkles.

Mesotherapy using the mechanism of tissue fibroplasia improves parameters of ageing skin, such as hydration level, thickness of the dermis, visibility of wrinkles, erythema, and skin discolouration.

Keywords: mesotherapy, succinic acid, hyaluronic acid, ultrasonography, echogenicity, tissue fibroplasia, biorevitalization, biostimulation, multispectral analysis

STRESZCZENIE

Fibroplazja tkankowa, czyli połączenie mechanizmu działania biorewitalizatora z biostymulatorem w jednym preparacie do mezoterapii, to stosunkowo nowa grupa produktów iniekcyjnych.

Celem pracy była ocena wpływu preparatu z kwasem hialuronowym i bursztynianem sodu na poprawę stanu skóry u kobiet o skórze suchej z wyraźnymi oznakami starzenia.

Wykazano istotny statystycznie spadek echogeniczności skóry w stosunku do stanu pierwotnego, zwiększenie grubości skóry oraz spłycenie pojedynczych zmarszczek.

Mezoterapia z wykorzystaniem mechanizmu fibroplazji tkankowej wpływa na poprawę parametrów starzejącej się skóry, takich jak poziom nawilżenia, grubość skóry właściwej, widoczność zmarszczek, rumień, czy przebarwienia skóry.

Słowa kluczowe: mezoterapia, kwas bursztynowy, kwas hialuronowy, ultrasonografia, echogeniczność, fibroplazja tkankowa, biorewitaizacja, biostymulacja, multispektralna analiza parametrów skóry

INTRODUCTION

Tissue fibroplasia is a mechanism that belongs to relatively new group of needle mesotherapy formulations, which combine the effects of both biorevitalizers and skin biostimulators. This makes it possible to simultaneously supply the extracellular matrix (ECM) with substances that are lost with age; replenish the skin's water reservoir, as well as stimulate anabolic processes of fibroblasts. Examples of fibroplasia include products containing both hyaluronic acid and succinic acid in the form of sodium succinate [1].

Hyaluronic acid (HA) can be in both forms, molecular and fragmented, in the formulation. Biorevitalization of the skin occurs after the application of molecular HA, which does not have the ability to interact with the CD-44 protein receptor on the fibroblast, unlike the fragmented form. It is responsible for replenishing the skin's water reservoir in order to provide an optimal environment for skin cell function. With molecular HA, it is possible to improve collagen synthesis, but it does not affect fibroblast proliferation itself [2].

Succinic acid is a natural modulator of cell metabolism involved in the Krebs cycle. Among other things, it is responsible for the biosynthesis and secretion of structural proteins - collagen and elastin, as well as the production of adenosine triphosphate (ATP). In addition, sodium succinate has a positive effect on angiogenesis and dermal microcirculation, thereby improving antioxidant processes in the skin. The existence of a receptor on fibroblasts for succinate has also been demonstrated. Thanks to the joint interaction of, there is proliferation and migration of fibroblasts, as well as stimulation of their secretory activity towards growth factors, chemokines and cytokines [3] .

The combination of molecular hyaluronic acid with sodium succinate enables to simultaneously provide an optimal environment for fibroblasts, improve their functioning and stimulate their proliferation. This synergy of action allows for effective counteracting of degenerative processes due to both endogenous aging and photoaging [4].

MATERIAL AND METHODS

Study group

The study included 12 women, phototype II-III according to Fitzpatrick , aged 30 to 60 years, living in a city >500,000 inhabitants, with dry skin with recognized signs of endogenous aging and photoaging. During the study, the proband's daily living conditions did not change.

Methodology

Before the start of the study, skin parameters of each of the women were measured on both the right and left cheek and as a control on the neck , which was not treated.

The study of skin parameters was multistage and included:

- ultrasonography of the skin with a 48 MHz probe frequency device with measurement of the echogenicity of the dermis (0-30 degrees of gray on a 256 degree gray scale, in an area of 4000 mm^2 in a precisely designated location: between points 18, 19, 23, 24 located on lines 17-20: 0.5 cm from the nasal lobe, a slightly curved line along the zygomatic bone, and 22-25: a slightly curved line from the center of the nasolabial fold to a point 1.5 cm away from the earlobe. Tissue echogenicity was shown as a ratio of LEP/TP (*low echogenicity pixels to total* pixels), i.e., low-reflectivity pixels to *total* pixels in the study area. A decrease in echogenicity correlates with increased tissue hydration (Fig. 1, Table 1) [5-7];
- multispectral skin analysis. The device for multispectral analysis of skin parameters uses 8 modules that allow objective assessment of skin condition on multiple levels. The test uses both modes based on daylight and UV light, Wood's lamp or parallel and cross-polarized light.

  Applied:

  1. for assessing skin texture (visibility of sebaceous gland outlets, wrinkles, or furrows): parallel polarized light and texture analysis mode;
  2. for assessing hyperpigmentation: UV radiation, Wood's lamp and hyperpigmentation analysis mode; for capillary evaluation: cross-polarized light and blood vessel analysis mode;
  3. for assessing skin hydration: a Wood's lamp and UV light. Scalar evaluation according to the *wrinkle severity rating* scale (WSRS). Palpation and visual assessment.

Subsequently, each of the 12 subjects received 6 treatments with a molecular hyaluronic acid-based preparation with sodium succinate (1%) (6 doses of 3 ml / session) using a point-by-point technique with a 32G 4 mm needle, from an angle of 15-30°, with an interval of 10 days between treatment sessions.

Skin parameters were measured again before the third treatment, before the fifth treatment and two weeks after the sixth treatment. In addition, treatment effects were assessed using the Glogau [8], WSRS [9], and Gais [10] scales, and satisfaction was examined women using a questionnaire based on the Linkert scale [11].

Prior to the treatment procedure, each of the subjects completed a medical questionnaire regarding contraindications to the procedures and were informed a about post-treatment precautions. As a condition for entering the research process, the subjects declared that they would not make any significant changes in their lifestyle or skin care that could affect skin parameters and interfere with the measurements taken strictly related to the process of verifying the effectiveness of the administered preparation and its direct effect on the skin.

Analysis of results

The results of skin echogenicity measurements were subjected to statistical analysis using Student's T-Test, considering results with $p<0.01$ as significant. In addition to this, percentage analysis methods were used.

A $\chi 2$ test for a significance level of 0.05 was used to assess the significance of the results of the questionnaires completed by the respondents.

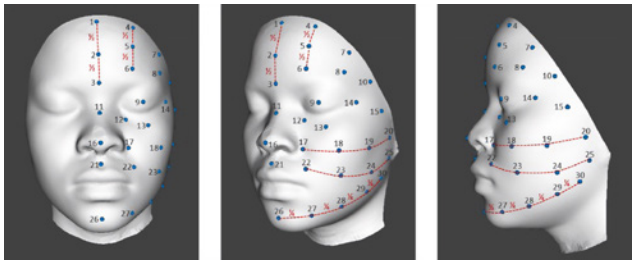

Fig. 1 Mapping layout. Front, oblique and lateral images of 30 predefined face measurement points **Source:** [7]

Table 1 Mapping layout. Description predefined face measurement points

Site #	Description of site	Localization of site
17	Nasolabial sulcus, top	0.5 cm left of nostril
18	Cheek, middle, oblique	In slightly curved line with 17, 19 and 20
19	Cheek, middle, oblique/lateral	In slightly curved line with 17, 18 and 20
20	Cheek, middle, lateral	In slightly curved line with 17, 18 and 19
21	Philtrum	Middle of upper up in cleft
22	Nasolabial sulcus, midpoint	Midpoint of nasolabial fold
23	Cheek, lower, oblique	In slightly curved line with 22, 24 and 25
24	Cheek, lower, oblique/lateral	In slightly curved line with 22, 23 and 25
25	Cheek, lower, lateral	In slightly curved line with 22, 23 and 24
26	Chin, central	Middle of chin
27	Jaw, anterior/oblique	Exactly between 26 and 28
28	Jaw, oblique	Exactly between 26 and 30
29	Jaw, oblique/lateral	Exactly between 28 and 30
30	Jaw, lateral	Slightly above mandibular angle

Source: [7]

RESULTS

Echogenicity measurement

There was a statistically significant decrease in the echogenicity of the tissue ($p<0.001$) after a series of 6 treatments with the test preparation (N=12). The results are shown in table 2.

Percentage analysis showed a decrease in echogenicity by an average of 36.2% from the original measurement (Table 3).

Ultrasonographic measurement of the thickness of the dermis

There was a statistically significant increase in the thickness of the dermis ($p<0.001$) after a series of 6 treatments with the test product (N=12). The results are shown in Table 4. Percentage analysis showed an increase in dermis thickness by an average of 11.5% from baseline (Table 5).

Table 2 Echogenicity measurement results

Echogenicity Measurement I [%]	Echogenicity. Measurement II [%]	Measurement difference	Mean difference	Square differences
7.54	4.11	3.43	1.188333333	1.412136111
4.67	3.64	1.03	-1.211666667	1.468136111
6.49	2.33	4.16	1.918333333	3.680002778
5.59	4.32	1.27	-0.971666667	0.944136111
4.29	3.15	1.14	-1.101666667	1.213669444
6.16	4.34	1.82	-0.421666667	0.177802778
5.78	3.01	2.77	0.528333333	0.279136111
6.89	4.78	2.11	-0.131666667	0.017336111
7.09	5.11	1.98	-0.261666667	0.068469444
5.43	2.99	2.44	0.198333333	0.039336111
6.09	2.01	4.08	1.838333333	3.379469444
4.32	3.65	0.67	-1.571666667	2.470136111
	Mean of differences	2.241666667	Sum of squares	15.14976667
			Sum of squares divided by the number of degrees of freedom	1.377251515
			Test result	6.62
			P-value	p<0.001

Source: Own elaboration

Table 3 Percentage analysis of echogenicity decrease

Ratio of echogenicity after the sixth procedure to the state before the procedure	Percentage	Percentage difference
0.545092838	54.50928382	45.49071618
0.779443255	77.94432548	22.05567452
0.359013867	35.90138675	64.09861325
0.772808587	77.28085868	22.71914132
0.734265734	73.42657343	26.57342657
0.704545455	70.45454545	29.54545455
0.520761246	52.07612457	47.92387543
0.693759071	69.37590711	30.62409289
0.720733427	72.07334274	27.92665726
0.550644567	55.06445672	44.93554328
0.330049261	33.00492611	66.99507389
0.844907407	**84.49074074**	**15.50925926**
0.734265734	73.42657343	26.57342657
	Mean	**36.228535**

Source: Own elaboration

Table 4 Results of dermis thickness measurement

Dermis thickness Measure I	Dermis thickness Measure II	Measure-ment difference	Mean difference	Square differences
0.94	1.14	-0.2	-0.0475	0.00225625
1.78	1.92	-0.14	0.0125	0.00015625
1.55	1.66	-0.11	0.0425	0.00180625
1.37	1.45	-0.08	0.0725	0.00525625
1.69	1.95	-0.26	-0.1075	0.01155625
1.01	1.23	-0.22	-0.0675	0.00455625
1.24	1.42	-0.18	-0.0275	0.00075625
1.67	1.78	-0.11	0.0425	0.00180625
1.54	1.6	-0.06	0.0925	0.00855625
1.45	1.59	-0.14	0.0125	0.00015625
1.31	1.5	-0.19	-0.0375	0.00140625
1.47	1.61	-0.14	0.0125	0.00015625
	Mean difference	-0.1525	Sum of squares	0.038425
			Sum of squares divided by the number of degrees of freedom	0.003493182
			Sum of squares divided by the number of degrees of freedom	0.000317562
			Test result	-8.94
			P-value	p<0.001

Source: Own elaboration

Table 5 Percentage analysis of dermis thickness

Ratio of dermis thickness after the sixth treatment to the state before the treatment	Percentage	Percentage difference
1.212765957	121.2765957	21.27659574
1.078651685	107.8651685	7.865168539
1.070967742	107.0967742	7.096774194
1.058394161	105.8394161	5.839416058
1.153846154	115.3846154	15.38461538
1.217821782	121.7821782	21.78217822
1.14516129	114.516129	14.51612903
1.065868263	106.5868263	6.586826347
1.038961039	103.8961039	3.896103896
1.096551724	109.6551724	9.655172414
1.145038168	114.5038168	14.50381679
1.095238095	109.5238095	9.523809524
	Average increase in thickness by	**11.49388385**

Source: Own elaboration

Comparison of ultrasound images

It showed a shallowing of individual wrinkles by an average of 0.02 mm, as well as a visible thickening of the dermis and a decrease in ultrasound image brightness.A control sample on the neck showed the same dermis thickness (1.72 mm) before and after six treatments .

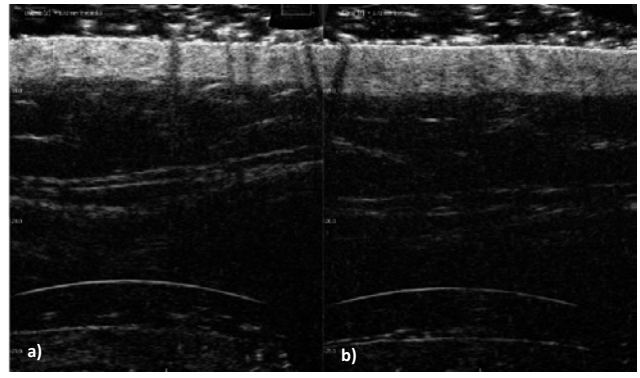

Fig. 2 Ultrasound image of the control sample: a) before the treatment session, b) after the sixth treatment. Thickness of the dermis on the neck

Source: Own archive

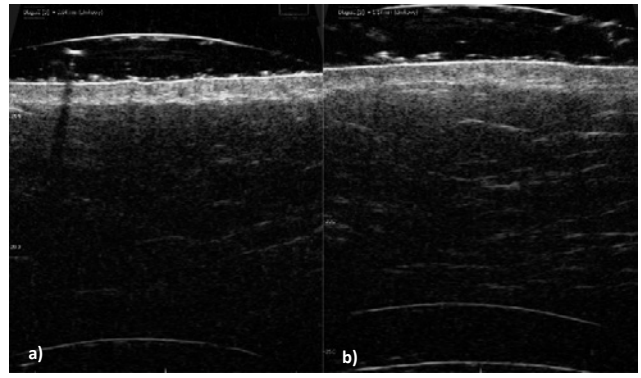

Fig. 3 Ultrasound image (a) before the treatment session, (b) after the sixth treatment. Change in the thickness of the dermis in the treatment area

Source: Own archive

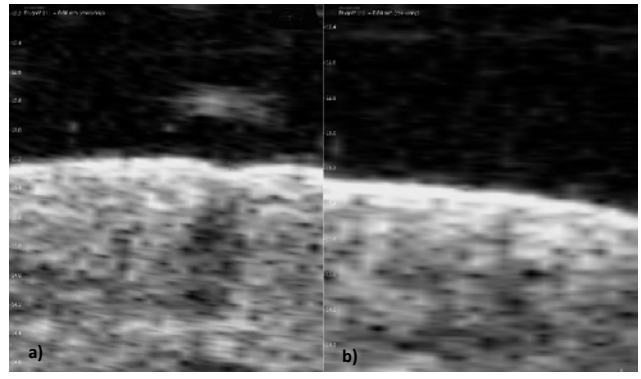

Fig. 4 Ultrasound image (a) before the treatment session, (b) after the sixth treatment. Change in the depth of the wrinkle in the treatment area in woman #3.

Source: Own archive

Multispectral analysis

Figures 5-9 shows the results of the comparative multispectral analysis.

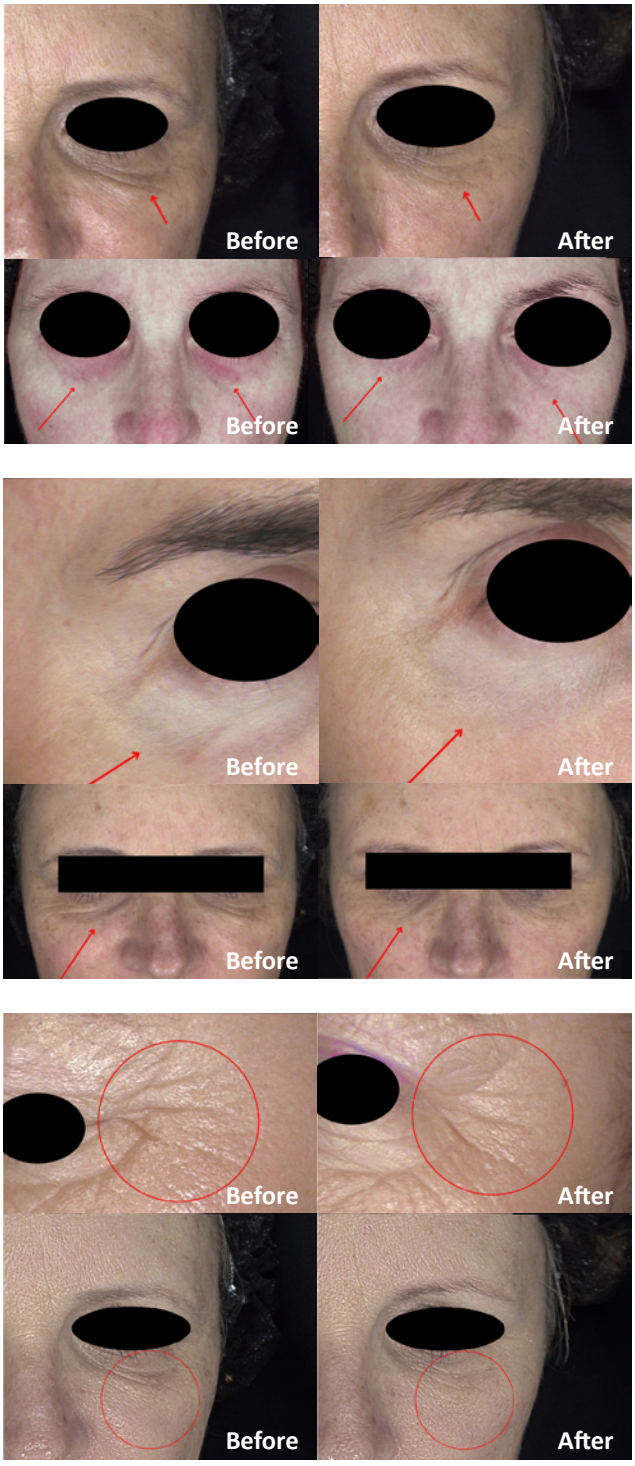

Fig. 5 Improving skin tone in the eye area **Source:** Own archive

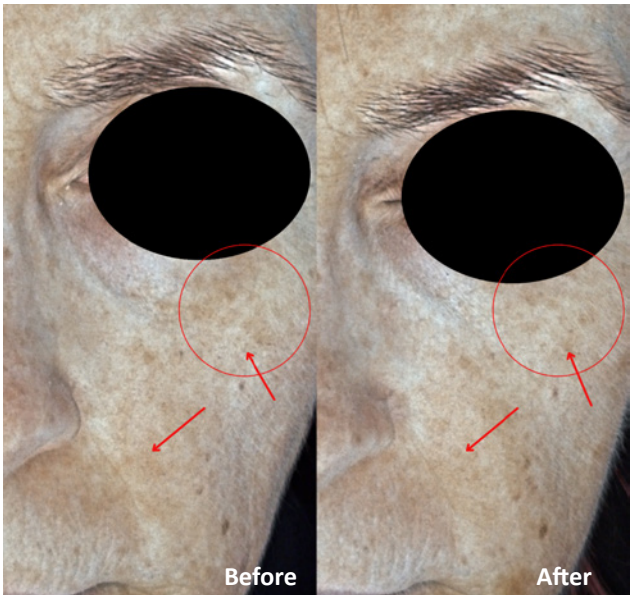

Fig. 6 Reduction of discoloration **Source:** Own archive

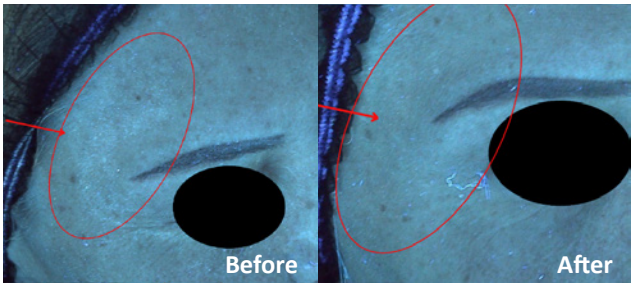

Fig. 7 Improved skin hydration (white area in Wood's lamp indicates dehydration) **Source:** Own archive

Fig. 8 Facial oval improvement **Source:** Own archive

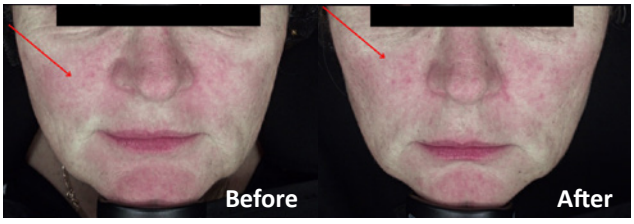

Fig. 9 Reduction of erythema **Source:** Own archive

Scalar effects evaluation

The scalar evaluation was performed by an independent expert before the treatment session and 2 weeks after the last treatment.

All subjects improved their skin condition by one type according to the Glogau scale. Evaluation with the GAIS scale showed an average improvement of grade 2 - significant improvement (Table 6).

Table 6 Evaluation of of women by GAIS scale

Woman's number	GAIS score	Woman's number	GAIS score
1	2	8	2
2	1	9	1
3	2	10	2
4	2	11	3
5	2	12	3
6	2	Mean	2
7	2		

Source: Own elaboration

Author's questionnaire based on the Linkert scale satisfaction rating

The questionnaire consisted of 10 closed-ended questions representing assertions, for which respondents were to indicate their degree of agreement, where:

1 - strongly disagree
2 - rather disagree
3 - I have no opinion
4 - rather agree
5 - strongly agree

Responses were analyzed using the $\chi 2$ statistical significance test for a significance level of 0.05. A statistically significant strong agreement was found on 4 skin parameters α=0.005 (N=12) - improved a hydration, improved skin tone, smoothed wrinkles, overall improved a skin quality, and respondents' satisfaction with the effects achieved.

There was a statistically significant degree of improvement in skin tone α=0.003 (N=12). 87% of respondents strongly agreed with the statement of visible skin tone equalization, and 13% selected the answer "rather agree". There was statistically significant satisfaction with the lightening of skin discoloration α=0.015 (N=12). 33% of respondents (N=12) strongly agreed with the statement that skin discoloration brightened noticeably after the treatment session. It is worth noting at this point that only 50% of respondents (N=12) had hyperpigmented lesions visible to the naked eye before the study.

Interestingly, 100% of the respondents have no opinion on the improvement of erythematous lesions. Their imaging in multispectral diagnostics provides a broader view than visual assessment alone. Vascular lesions are definitely more visible with instrumental diagnostics. Although respondents have no opinion on their improvement, cross-polarized light imaging shows a clear improvement.

CONCLUSIONS

The use of the mechanism of tissue fibroplasia in anti-aging mesotherapy brings clear, measurable results. Thanks to the combination of molecular hyaluronic acid with succinic acid, the hydration level of the dermis is increased and thickening of the dermis occurs, as indicated by ultrasound measurement. The stimulating effect of sodium succinate contributes to the reduction of wrinkles and thickening of the dermis, which is particularly evident in the eye area. In addition, a reduction in hyperpigmentation and erythema has been shown.

In addition to measurable, objective results, therapy using the mechanism of tissue fibroplasia enables to achieve results visible to the naked eye in a relatively short period of time, which translates into a level of satisfaction among those who have received treatments.

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