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Research Article

Unique Retinol Therapy with Antioxidant and Anti-Inflammaging Complex for Naturally Reborn Skin: The Clinical Case Series Study

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One of the methods used to prevent symptoms of skin aging are chemical peels. Among retinoids, retinol is much less described in the literature than tretinoin as a substance used in the peel procedure. The aim of our study was to determine the efficacy of using a 4% retinol solution product containing novel TGF-β activators and antioxidants in improving the condition of the skin in patients with facial skin issues caused by aging and skin disorders. Each of 15 patients went through three peel treatment series, with a 30-day gap between each session and was examined using Multi Skin Test MC 1000 Courage + Khazaka, evaluating hydration, elasticity, and skin pigmentation and Observ 520x. All patients reported overall improvement after the peeling procedure, and most of them reported subjective improvement in the reduction of the facial skin: tone, skin pigmentation, dehydration, dryness, structure, and sebaceous gland activity. An objective evaluation revealed significant clinical improvement in pigmentation in study groups. Elasticity parameters were shown to increase during treatment, with a greater effect occurring in patients with mature skin with first signs of aging and patients with postinflammatory hyperpigmentation, atrophic acne scars, and enlarged pores. Concluding, combined peel therapy of 4% retinol serum product containing novel TGF-β activators and antioxidants showed good efficacy in reducing facial pigmentation of the skin high patients' satisfaction with the procedure. The study revealed that the described method is simple to use, has low cost, is with rare adverse events, and has well tolerability.

1. Introduction

The skin is the largest single organ in the human body with a surface area of around 2 m^2 and a mass of 15% of the total body mass [1]. The main functions of the skin include regulating body temperature, protecting the organism from mechanical injuries and infections, and ensuring water-electrolyte management. Despite these very important functions, it also has an important cosmetic role. It is known that young-looking skin and appearance may have a positive influence on people's social behavior [2–4]. According to the literature, factors such as age, skin diseases, and exposure to sunlight may change the skin condition. With age, the skin becomes thinner and progressively less hydrated, mostly due to a reduction in the quantity of natural moisturizers [5, 6]. Over the years, as a result of the declining collagen synthesis in the dermis and the resilience of its already-existing collagen and elastin fibers, the skin also loses its elasticity. These processes defined by the clinical, histological, and physiological decrements that occur in the sun-protected skin are called in the literature as intrinsic aging [5, 7–9]. The second factor causing skin aging is long-term exposure to sunlight which belongs to extrinsic aging factors. It commonly manifests as pigmentation changes (hypopigmentation or hyperpigmentation), rough skin, dryness, telangiectasias, and wrinkles [9–11]. Histologically, these are the result of alterations in dermal connective tissue, accumulation of disorganized elastin, its microfibrillar component fibrillin in the deep layers of the dermis, and acute loss of interstitial collagen [12].

One of the methods used to prevent symptoms of skin aging are chemical peels [13]. These are divided into superficial, medium-depth, and deep kinds, based on how deeply they penetrate the skin. Not only the substance but also its concentration, pH of the solution, and time of application have an impact on the procedure effects [14]. Commonly used superficial peels include tretinoin, salicylic acid, Jessner solution, and also glycolic and pyruvic acid. They target the epidermis and the epidermal-dermal interface, causing decreased corneocyte adhesion, epidermolysis, and increased dermal collagen deposition [15]. Retinol (vitamin A, all-trans-retinol) is much less described in the literature than tretinoin as a substance used in the peel procedure. Retinol was proven to be effective in reducing wrinkles, loss of skin elasticity, and pigmentation; nonetheless, the evidence is weak [16–20].

The aim of our study was to determine the efficacy of using a 4% retinol solution product containing novel TGFβ activators and antioxidants in improving the condition of the skin in patients with facial skin issues caused by aging and skin disorders.

2. Materials and Methods

2.1. Study Design. The study was conducted between August 2022 and December 2022. It was approved by the Independent Bioethics Committee for Scientific Research at the Medical University of Gdansk, Poland (NKBBN/618/2022). Prior to the study, each patient supplied written informed consent. In total, 15 healthy women were enrolled according to inclusion and exclusion criteria and qualified into three groups conforming to facial skin problems as follows:

(i) Group S: 5 patients with mature skin with first signs of aging (such as fine lines and wrinkles and dry and dehydrated skin)

(ii) Group P: 5 patients with superficial and deep hyperpigmentation (such as melasma and sun spots)

(iii) Group NSS: 5 patients with postinflammatory hyperpigmentation, atrophic acne scars, and enlarged pores.

Patients from each group were subjected to chemical peel sessions according to the same protocol, indicated by the producer. Each patient had three peel treatment series, with a 30-day gap between each session. Throughout the research, they were required to utilize the same daily maintenance and photoprotection cosmetic items provided by the creator. Before the treatment series and before each peel session during the treatment day, patients were examined using Multi Skin Test MC 1000 Courage + Khazaka, evaluating hydration, elasticity, and skin pigmentation; Observ 520x and dermatoscope. The last examination with the measurement above parameters was performed 30 days after the last peel procedure. In total, the patients were examined 5 times.

Before the study, patients were asked, with the option to answer yes or no, regarding the occurrence of several subjective facial skin symptoms among others: itching, burning, roughness, redness, exfoliation, and tightness. After the peel treatment series, they subjectively assessed the achieved improvement, according to the symptoms: redness, skin tone, dehydration skin pigmentation, dryness, wrinkles, structures, sebaceous gland activity, scar, and overall improvement. Patients assessed the reduction of the abovementioned symptoms as an answer: yes; slightly; no.

2.2. Inclusion Criteria

(i) Women with I-III Fitzpatrick skin type including features such as first signs of aging, mature skin, shallow discoloration, postinflammatory discoloration, acne scars, dilated sebaceous glands, and uneven texture.

(ii) Age: 35–50 years

(iii) Sex: women

(iv) Good health condition

(v) Signed informed consent.

2.3. Exclusion Criteria

(i) Pregnancy

(ii) Breastfeeding period

(iii) Open wounds, violation of the continuity of the epidermis

(iv) Hypersensitivity to any of the preparation ingredients

(v) Acute and chronic infectious processes, e.g., tuberculosis, active herpes simplex virus infection

(vi) Use of isotretinoin in the last 6 months

(vii) Epilepsy

(viii) Emotional instability

(ix) Facial surgery in the last 6 months

(x) Tendency to keloids

(xi) Occurrence of skin diseases: rosacea, acne tarda, atopic dermatitis, contact dermatitis, and seborrheic dermatitis.

2.4. Procedure of Chemical Peeling. The chemical peeling procedure was performed in the Department of Dermatology, according to the producer's protocol. The area of the procedure was well ventilated, and patients' eyes were covered during the peeling procedure to avoid irritation. At first, make-up removal of the skin was made after which the skin was treated with a degreasing agent, Retix.C PRE-PEEL. Subsequently, one ampoule of Retix.C BOOSTER serum was applied over the face surface and left until complete absorption. Next, the contents of the vial of Retix.C Retinol TGF Activator were spread with a brush over the entire surface of the face. The solution was left on the skin for 6 hours, after which it was washed off with lukewarm water.

After the procedure patients were asked to use daily skin care: Ultra Repair Moisturizer and SPF50+ cream in the morning and Retimodeling serum for oily and Anti-Aging Face Cream Retix C for dry skin in the evening.

2.5. Products. The chemical peeling procedure was performed using two products. Firstly, an antioxidant product Retix C BOOSTER Serum was applied on the facial skin; subsequently, patients were treated with Retix C Retinol TGF Activator, containing 4% retinol and TGF activators.

2.6. Statistical Analysis. Completed surveys were downloaded for statistical analysis. The collected data were analyzed in Statistica 12.0 software. The Shapiro–Wilk W test was used to check whether the quantitative variable came from a normally distributed population. The Leven (Brown–Forsythe) test was used to test the hypothesis of equal variances. The significance of differences between more than two groups was tested by F (ANOVA) or Kruskal–Wallis test. In case of statistically significant differences between the groups, post hoc tests were used (Tukey's test for F, Dunn's test for Kruskal–Wallis). The significance of differences between more than two in the linked variable model was checked by repeated measures analysis of variance or Friedman's test. Chi-square tests were used for qualitative variables (using Yates correction for cell counts below 10, checking Cochran conditions, and Fisher's exact test, respectively). A p value equal to or less than 0.05 was considered statistically significant.

3. Results

A total of 15 patients (all females), with age range 37–50 (mean age: 41) completed the study. Subjective evaluation, according to the survey data collected during the last peel session, showed a good efficacy of the therapy. Most of the patients reported improvement in the reduction of the facial skin: uneven tone, skin pigmentation, dehydration, dryness, uneven structure, and sebaceous gland activity. All patients reported overall improvement after the peeling procedure. No improvement was reported in the following symptoms: redness, liquidation of pigmentations, wrinkle reduction and liquidation, as well as scar reduction and liquidation (Table 1).

An objective evaluation revealed a significant clinical improvement in pigmentation overall in study groups, specifically in patients with mature skin with first signs of aging (Table 2) (Figure 1). Elasticity parameters were shown to increase during treatment, with a greater effect occurring in patients with mature skin with first signs of aging and patients with postinflammatory hyperpigmentation, atrophic acne scars, and enlarged pores; however, none of the differences were statistically significant (Table 3) (Figure 2). Furthermore, there was no improvement noticed referring to the hydration of the skin during the therapy (Table 1) (Figure 3). Improvement of skin condition as photo documentation in groups P, S, and NSS is shown in Figures 4–6, respectively.

3.1. Adverse Events. There were no serious adverse events in patients during the study. Only one patient reported mild itching during skin exfoliation, and the same patient noticed dryness of the skin after the procedure.

4. Discussion

Vitamin A was first found in about 1906 and synthesized in 1947 [21]. Since then, research on the use of retinol in medical indications has been underway. Its effectiveness in terms of antiaging was first suggested by Kang S. et al., who demonstrated, similarly to retinoic acid, the administration of all-trans-retinol to normal human skin effects on epidermal thickening and increases the expression of CRABP II and CRBP mRNAs and proteins. The scientists also noted that, in contrast to tretinoin, retinol caused very little erythema and discomfort.

Literature regarding the efficacy of retinol used as a peeling substance seems to be poor yet promising. Wojcik et al. investigated the effects of 2% retinol peel on skin lipids in the face and neck area. The authors observed a significant growth of sebum on the left cheek, nose, chin, and left side of the neck. The methods used were similar to ours. The 2% retinol chemical peel was applied 3 times in 3 weeks of intervals in 21 women. However, there was no other parameter investigated besides sebum secretion [22]. In another study by Sadick et al., 24 patients (photodamage group, $n = 14$ (with an acne subgroup, $n = 5$]; melasma group, $n = 5$; skin of color, $n = 5$) were treated with 3% retinol peel in 6 weeks of intervals and a series of 2–4 peels. Nonetheless, only the photodamage group was evaluated. Dermatologist clinical grading of fine lines, wrinkles, pore size, laxity, mottled pigmentation, lack of clarity/radiance, and overall photodamage was significantly improved ($P < 0.05$) In comparison to our study, in that research efficacy was evaluated mainly based on the dermatologist; thus, the results might be not fully objective [23].

The study group of our research consisted of patients only with Fitzpatrick I-III skin type. Furthermore, there is currently no research investigating the effectiveness of retinol chemical peel in the dark skin population. However, the effectiveness of other chemical peel substances has been described in the literature. The systematic review and meta-analysis of comparative trials by Dorgham et al. reported satisfactory results of glycolic acid (GA) and trichloroacetic acid peel as a melasma treatment in dark skin patients, with better effects and safety profile of GA. Undoubtedly, there is a need to perform research evaluating the effectiveness of retinol peel in the population with Fitzpatrick IV-VI skin type [24].

According to the literature, transforming growth factor, beta (TGF-beta), plays a crucial role in regulating the extracellular matrix (ECM), which becomes remodeled in the aging skin, including photoaging. TGF-beta regulates the differentiation of the epidermal layer by inhibiting the growth of epithelial cells. On the other hand, it promotes fibroblast proliferation in connective tissue and thus has an impact on type I procollagen production by TGF-beta type II receptor activation [25–27]. Therefore, well-balanced TGF-β

Table 1: Patients' subjective assessment of facial skin symptom changes.

	P ($n = 5$)	S ($n = 5$)	NSS ($n = 5$)	Summary ($n = 15$)
Redness				
Yes	1 (20.0%)	2 (40.0%)	3 (75.0%)	6 (42.9%)
Slightly	2 (40.0%)	3 (60.0%)	0 (0.0%)	5 (35.7%)
No	2 (40.0%)	0 (0.0%)	1 (25.0%)	3 (21.4%)
Skin tone				
Yes	4 (80.0%)	4 (80.0%)	4 (80.0%)	12 (80.0%)
Slightly	1 (20.0%)	1 (20.0%)	1 (20.0%)	3 (20.0%)
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin pigmentation reduction				
Yes	4 (80.0%)	4 (80.0%)	4 (80.0%)	12 (80.0%)
Slightly	1 (20.0%)	1 (20.0%)	1 (20.0%)	3 (20.0%)
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin pigmentation liquidation				
Yes	1 (20.0%)	3 (75.0%)	2 (40.0%)	6 (42.9%)
Slightly	3 (60.0%)	1 (25.0%)	1 (20.0%)	5 (35.7%)
No	1 (20.0%)	0 (0.0%)	2 (40.0%)	3 (21.4%)
Dehydration				
Yes	3 (60.0%)	3 (60.0%)	4 (80.0%)	10 (66.7%)
Slightly	1 (20.0%)	1 (20.0%)	0 (0.0%)	2 (13.3%)
No	1 (20.0%)	1 (20.0%)	1 (20.0%)	3 (20.0%)
Dryness				
Yes	2 (40.0%)	3 (75.0%)	4 (80.0%)	9 (64.3%)
Slightly	2 (40.0%)	1 (25.0%)	0 (0.0%)	3 (21.4%)
No	1 (20.0%)	0 (0.0%)	1 (20.0%)	2 (14.3%)
Wrinkle reduction				
Yes	2 (40.0%)	3 (60.0%)	0 (0.0%)	5 (33.3%)
Slightly	3 (60.0%)	2 (40.0%)	2 (40.0%)	7 (46.7%)
No	0 (0.0%)	0 (0.0%)	3 (60.0%)	3 (20.0%)
Wrinkle liquidation				
Yes	0 (0.0%)	2 (40.0%)	0 (0.0%)	2 (13.3%)
Slightly	2 (40.0%)	3 (60.0%)	0 (0.0%)	5 (33.3%)
Nie	3 (60.0%)	0 (0.0%)	5 (100.0%)	8 (53.4%)
Structure				
Yes	5 (100.0%)	4 (80.0%)	3 (60.0%)	12 (80.0%)
Slightly	0 (0.0%)	1 (20.0%)	2 (40.0%)	3 (20.0%)
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sebaceous gland activity				
Yes	3 (60.0%)	3 (60.0%)	3 (60.0%)	9 (60.0%)
Slightly	0 (0.0%)	1 (20.0%)	2 (40.0%)	3 (20.0%)
No	2 (40.0%)	1 (20.0%)	0 (0.0%)	3 (20.0%)
Scar reduction				
Yes	1 (33.3%)	1 (25.0%)	2 (40.0%)	4 (33.3%)
Slightly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
No	2 (66.7%)	3 (75.0%)	3 (60.0%)	8 (66.7%)
Scar liquidation				
Yes	0 (0.0%)	0 (0.0%)	1 (20.0%)	1 (9.1%)
Slightly	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (9.1%)
No	2 (66.7%)	3 (100.0%)	4 (80.0%)	9 (81.8%)
Overall improvement				
Yes	5 (100.0%)	5 (100.0%)	5 (100.0%)	15 (100.0%)
Slightly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
After which series improvement was noticed				
1	0 (0.0%)	2 (40.0%)	1 (20.0%)	3 (20.0%)
2	3 (60.0%)	3 (60.0%)	2 (40.0%)	8 (53.3%)
3	2 (40.0%)	0 (0.0%)	2 (40.0%)	4 (26.7%)
After which series skin peeling was noticed				
1	0 (0.0%)	1 (20.0%)	0 (0.0%)	1 (7.7%)
2	2 (40.0%)	2 (40.0%)	2 (66.7%)	6 (46.2%)
3	1 (20.0%)	0 (0.0%)	1 (33.3%)	2 (15.4%)

Table 1: Continued.

	P ($n = 5$)	S ($n = 5$)	NSS ($n = 5$)	Summary ($n = 15$)
1, 2, 3	2 (40.0%)	2 (40.0%)	0 (0.0%)	4 (26.7%)
1, 3	0 (0.0%)	0 (0.0%)	1 (20.0%)	1 (6.7%)
2, 3	0 (0.0%)	0 (0.0%)	1 (20.0%)	1 (6.7%)

P: patients with superficial and deep hyperpigmentation, S: patients with mature skin with first signs of aging, NSS: patients with postinflammatory hyperpigmentation, atrophic acne scars, and enlarged pores.

Table 2: Skin pigmentation reduction during the therapy, with a statistically significant difference in group S.

	P ($n = 5$)	S ($n = 5$)	NSS ($n = 5$)	Summary ($n = 15$)
Test 1				
Mean (SD)	12.4 (2.2)	12.8 (2.6)	13.2 (1.7)	12.8 (2.1)
Range	10.8–15.5	8.5–14.7	11.5–15.3	8.5–15.5
Median	11.0	14.3[a]	12.3	12.3[a,b]
95% CI	[9.7; 15.0]	[9.6; 16.1]	[11.0; 15.3]	[11.6; 13.9]
Test 2				
Mean (SD)	12.3 (2.9)	11.5 (2.8)	13.0 (0.9)	12.3 (2.3)
Range	9.7–16.0	7.0–14.7	11.7–14.3	7.0–16.0
Median	10.7	11.8	13.0	12.3[c]
95% CI	[8.7; 16.0]	[8.0; 14.9]	[11.8; 14.2]	[11.0; 13.6]
Test 3				
Mean (SD)	11.7 (2.8)	10.9 (1.7)	10.9 (1.2)	11.2 (1.9)
Range	8.5–14.7	8.3–12.3	9.5–12.3	8.3–14.7
Median	11.7	11.0	11.0	11.0
95% CI	[8.2; 15.2]	[8.8; 13.0]	[9.3; 12.4]	[10.1; 12.2]
Test 4				
Mean (SD)	11.5 (2.3)	10.6 (1.4)	10.3 (1.6)	10.7 (1.7)
Range	9.5–14.3	9.5–13.0	7.8–11.7	7.8–14.3
Median	11.1	10.0	10.3	10.2[a]
95% CI	[7.8; 15.2]	[8.8; 12.4]	[8.3; 12.2]	[9.8; 11.7]
Test 5				
Mean (SD)	11.1 (2.5)	9.5 (2.3)	9.2 (2.0)	10.0 (2.3)
Range	8.3–13.7	5.7–12.0	7.3–12.0	5.7–13.7
Median	11.7	10.0[a]	8.5	10.0[b,c]
95% CI	[8.0; 14.3]	[6.6; 12.4]	[6.7; 11.7]	[8.7; 11.2]
p value	0.3793[2]	0.0221[2] [a]<0.05[3]	>0.05[2]	<0.0001[2] [a–c]<0.05[3]

P: patients with superficial and deep hyperpigmentation, S: patients with mature skin with first signs of aging, NSS: patients with postinflammatory hyperpigmentation, atrophic acne scars, and enlarged pores.

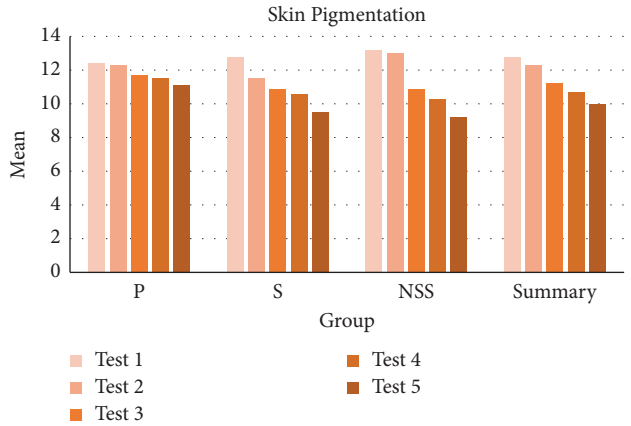

Figure 1: Skin pigmentation reduction during the therapy, with a statistically significant difference in group S. P: patients with Superficial and deep hyperpigmentation, S: patients with mature skin with first signs of aging, NSS: patients with postinflammatory hyperpigmentation, atrophic acne scars, and enlarged pores.

Table 3: Skin elasticity changes during the therapy.

	P ($n = 5$)	S ($n = 5$)	NSS ($n = 5$)	Summary ($n = 15$)
Test 1				
Mean (SD)	58.8 (11.0)	49.2 (14.8)	54.8 (4.9)	54.3 (11.0)
Range	48.0–76.0	35.0–73.0	50.0–60.0	35.0–76.0
Median	54.0	43.0	53.0	53.0
95% CI	[45.1; 72.5]	[30.9; 67.5]	[48.8; 60.8]	[48.2; 60.3]
Test 2				
Mean (SD)	56.8 (11.4)	52.0 (13.0)	48.8 (7.0)	52.5 (10.6)
Range	44.0–68.0	37.0–66.0	38.0–55.0	37.0–68.0
Median	62.0	49.0	49.0	49.0
95% CI	[42.6; 71.0]	[35.8; 68.2]	[40.1; 57.5]	[46.7; 58.4]
Test 3				
Mean (SD)	55.8 (12.9)	58.4 (16.6)	47.8 (11.7)	54.0 (13.7)
Range	40.0–68.0	45.0–87.0	37.0–62.0	37.0–87.0
Median	62.0	53.0	45.0	53.0
95% CI	[39.8; 71.8]	[37.8; 79.0]	[33.3; 62.3]	[46.4; 61.6]
Test 4				
Mean (SD)	56.5 (10.1)	69.4 (21.4)	51.6 (14.7)	59.4 (17.2)
Range	43.0–67.0	46.0–95.0	33.0–69.0	33.0–95.0
Median	58.0	74.0	58.0	58.0
95% CI	[40.5; 72.5]	[42.9; 95.9]	[33.3; 69.9]	[49.4; 69.3]
Test 5				
Mean (SD)	69.8 (8.1)	59.6 (13.2)	59.8 (13.1)	63.1 (11.9)
Range	58.0–78.0	45.0–79.0	48.0–82.0	45.0–82.0
Median	71.0	61.0	55.0	61.0
95% CI	[59.8; 79.8]	[43.2; 76.0]	[43.5; 76.1]	[56.5; 69.7]
p value	0.7032[2]	0.1097[2]	0.9585[2]	0.5245[2]

P: patients with superficial and deep hyperpigmentation, S: patients with mature skin with first signs of aging, NSS: patients with postinflammatory hyperpigmentation, atrophic acne scars, and enlarged pores.

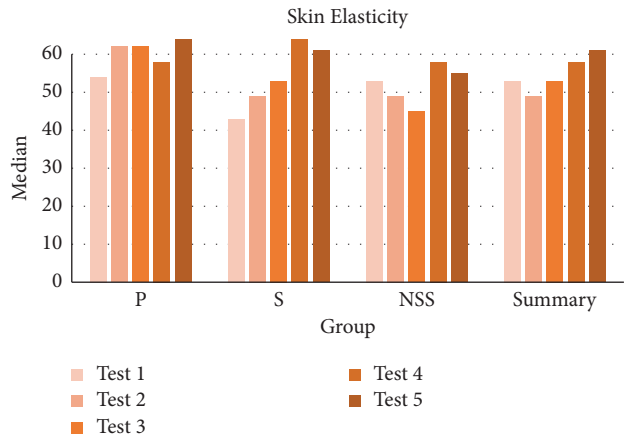

Figure 2: Skin elasticity changes during the therapy. P: patients with Superficial and deep hyperpigmentation, S: patients with mature skin with first signs of aging, NSS: patients with post-inflammatory hyperpigmentation, atrophic acne scars, and enlarged pores.

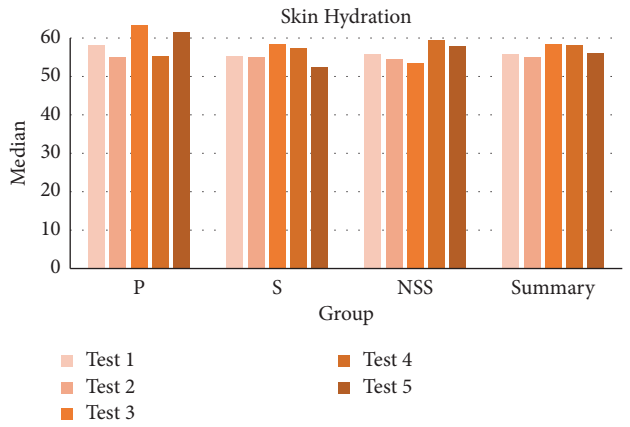

Figure 3: Skin hydration changes during the therapy. P: patients with Superficial and deep hyperpigmentation, S: patients with mature skin with first signs of aging, NSS: patients with post inflammatory hyperpigmentation, atrophic acne scars. and enlarged pores.

signaling is important to keep the skin in a healthy condition and support the maintenance of a young appearance. Given the cited literature data, studied chemical peel products contain novel substances which are the activators of the transforming growth factor, beta. To the best of our knowledge, it is the first study describing the effects of chemical peel containing the transforming growth factor, beta activators. Nevertheless, as a component of topical cosmeceuticals, they have been under investigation for a couple of years. The current literature suggests that topically applied growth factors in clinical contexts have a rejuvenation effect on the skin; notwithstanding, there is a high need for further studies confirming the thesis [28–30].

Structures providing structural integrity and resilience in the skin are called collagen fibrils, mainly composed of type I collagen (COL1) [31]. Due to natural aging and photoaging,

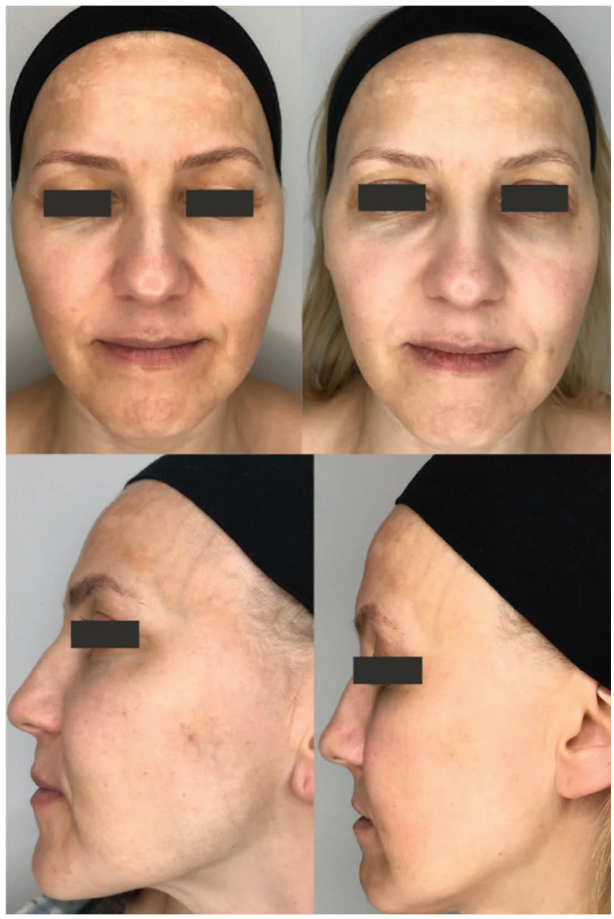

Figure 4: Photo of the patient from group P (patients with superficial and deep hyperpigmentation) before (left site) and after (right site) the peel treatment.

Figure 5: Photo of the patient from group S (patients with mature skin with first signs of aging) before (left site) and after (right site) the peel treatment.

the content of skin COL1 declines with the passage of time. This in turn results in the loss of elasticity, thinning, and wrinkling of the skin which contributes to an elderly appearance. Thus, restoration of collagen 1 synthesis and ultimately its content in the skin could contribute to enhancing the skin's resistance and firmness. It has been proven that retinol has a positive effect on metabolism of collagen which impacts the skin aging [17, 32]. Topical retinol restores Type I collagen production in the photoaged forearm skin within four weeks. Interestingly, Varani et al. postulated that, with increasing age, MMP levels are increased which can mediate a destruction of collagen [17]. Retinol, on the other hand, inhibits UV induction of MMP and stimulates collagen synthesis in the skin. Hence, by MMP inhibition, topical retinol has the ability to suppress degradation of newly synthesized procollagen and as a result leads to enhanced procollagen expression. Taking into consideration the use of retinol in skin care products for daily use, confirmed in numerous studies, it can be concluded that retinol is effective in treating aging and photoaging of the skin [9].

What is more, retinol has been also shown to have skin brightening properties. In 2003, Yoshimura et al. investigated the efficiency and adverse effects of 10% all-trans retinol (ROL) gel for improvement of skin hyperpigmentation [33]. The authors enrolled 21 Japanese patients with hyperpigmented lesions on the face. After more than 10 weeks of a follow-up, 18 patients were analyzed. Sixteen out of eighteen analyzed subjects showed improvement of pigmentation after an average treatment period of 11.3 weeks. Pigmentation was almost totally eliminated in 6 of the treated subjects. Reported side effects included erythema and scaling. It was concluded by the authors that ROL has the ability to improve skin hyperpigmentation as effectively as tretinoin when used at high concentration. Other studies, however using retinol in combination, also confirmed the abovementioned thesis [34, 35].

5. Limitations

The main limitations of the study were the small sample size and carrying out of the research in a single center, which was caused by the preliminary character of the research. However, the number of study participants remains equal to another comparable research. [36] Another limitation was the assessment of the effects no later than 3 weeks after the last peeling treatment and lack of the control group; therefore, there is a need to evaluate longer periods in further studies.

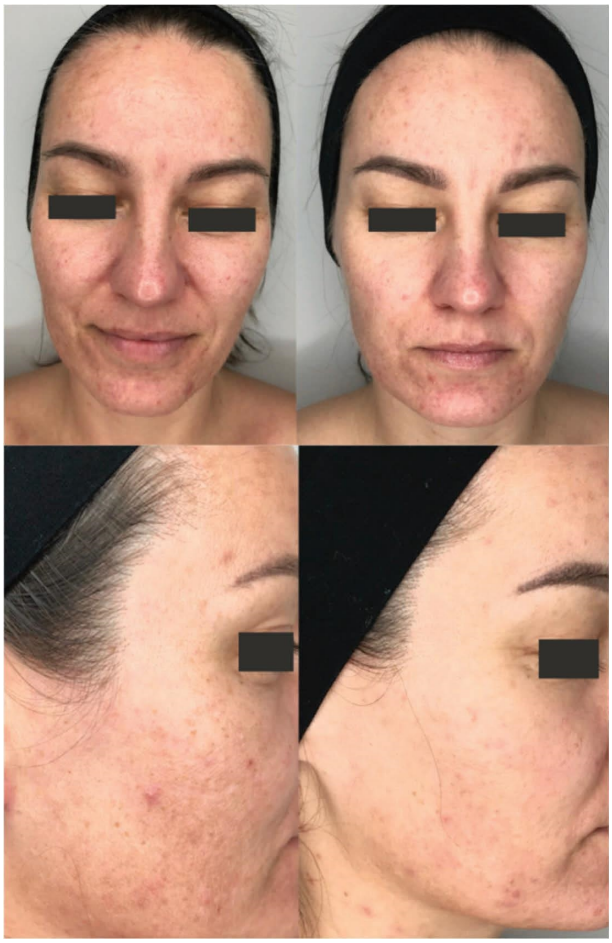

Figure 6: Photo of the patient from group NSS (patients with postinflammatory hyperpigmentation, atrophic acne scars, and enlarged pores) the peel treatment.

6. Conclusions

Combined peel therapy of 4% retinol serum product containing novel TGFβ activators and antioxidants showed good efficacy in reducing facial pigmentation of the skin. Despite the fact that there were no statistically significant results in improvement of skin hydration and elasticity, subjectively all patients showed high satisfaction with the procedure. The study revealed that the described method is simple to use, has low cost, is with rare adverse events, and has well tolerability. The next step will be a randomized control trial with an expanded study group to investigate the efficacy of therapy on discussed facial skin parameters.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Ethical Approval

The study was approved by the Independent Bioethics Committee for Scientific Research at the Medical University of Gdansk, Poland (NKBBN/618/2022).

Consent

Patient consent was acquired.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Study conception and design were conducted by D. Sołdacka, M. Podgórska, and W. Barańska-Rybak; data analysis was performed by D. Sołdacka, M. Podgórska, and W. Barańska-Rybak; literature review and study results' interpretation were performed by D. Sołdacka, M. Podgórska, and W. Barańska-Rybak; preparation of the final manuscript draft and editing were performed by D. Sołdacka, M. Podgórska, and W. Barańska-Rybak.

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References

[1] M. Rauma, A. Boman, and G. Johanson, "Predicting the absorption of chemical vapours," *Advanced Drug Delivery Reviews*, vol. 65, no. 2, pp. 306–314, 2013.

[2] A. K. Dąbrowska, G. Rotaru, S. Derler et al., "Materials used to simulate physical properties of human skin," *Skin Research and Technology*, vol. 22, no. 1, pp. 3–14, 2016.

[3] C. Blanpain and E. Fuchs, "Epidermal stem cells of the skin," *Annual Review of Cell and Developmental Biology*, vol. 22, no. 1, pp. 339–373, 2006.

[4] L. A. Zebrowitz and J. M. Montepare, "Social psychological face perception: why appearance matters," *Social and Personality Psychology Compass*, vol. 2, no. 3, pp. 1497–1517, 2008.

[5] A. Firooz, B. Sadr, S. Babakoohi et al., "Variation of biophysical parameters of the skin with age, gender, and body region," *The Scientific World Journal*, vol. 2012, Article ID 386936, 5 pages, 2012.

[6] M. Q. Man, S. Xin, S. Song et al., "Variation of skin surface pH, sebum content and stratum corneum hydration with age and gender in a large Chinese population," *Skin Pharmacology and Physiology*, vol. 22, no. 4, pp. 190–199, 2009.

[7] A. B. Cua, K. P. Wilhelm, and H. I. Maibach, "Elastic properties of human skin: relation to age, sex, and anatomical region," *Archives of Dermatological Research*, vol. 282, no. 5, pp. 283–288, 1990.

[8] H. S. Ryu, Y. H. Joo, S. O. Kim, K. C. Park, and S. W. Youn, "Influence of age and regional differences on skin elasticity as measured by the Cutometer," *Skin Research and Technology*, vol. 14, no. 3, pp. 354–358, 2008.

[9] S. Mukherjee, A. Date, V. Patravale, H. C. Korting, A. Roeder, and G. Weindl, "Retinoids in the treatment of skin aging: an overview of clinical efficacy and safety," *Clinical Interventions in Aging*, vol. 1, no. 4, pp. 327–348, 2006.

[10] M. Yaar, M. S. Eller, and B. A. Gilchrest, "Fifty years of skin aging," *Journal of Investigative Dermatology-Symposium Proceedings*, vol. 7, no. 1, pp. 51–58, 2002.

[11] B. A. Gilchrest, "Skin aging and photoaging: an overview," *Journal of the American Academy of Dermatology*, vol. 21, no. 3, pp. 610–613, 1989.

[12] K. Scharffetter-Kochanek, P. Brenneisen, J. Wenk et al., "Photoaging of the skin from phenotype to mechanisms," *Experimental Gerontology*, vol. 35, no. 3, pp. 307–316, 2000.

[13] R. Ganceviciene, A. I. Liakou, A. Theodoridis, E. Makrantonaki, and C. C. Zouboulis, "Skin anti-aging strategies," *Dermato-Endocrinology*, vol. 4, no. 3, pp. 308–319, 2012.

[14] T. C. Fischer, E. Perosino, F. Poli, M. S. Viera, and B. Dreno, "Chemical peels in aesthetic dermatology: an update 2009," *Journal of the European Academy of Dermatology and Venereology*, vol. 24, no. 3, pp. 281–292, 2010.

[15] M. I. Rendon, D. S. Berson, J. L. Cohen, W. E. Roberts, I. Starker, and B. Wang, "Evidence and considerations in the application of chemical peels in skin disorders and aesthetic resurfacing," *The Journal of Clinical and Aesthetic Dermatology*, vol. 3, no. 7, pp. 32–43, 2010.

[16] R. Kafi, H. S. R. Kwak, W. E. Schumacher et al., "Improvement of naturally aged skin with vitamin A (retinol)," *Archives of Dermatology*, vol. 143, no. 5, pp. 606–612, 2007.

[17] J. Varani, R. L. Warner, M. Gharaee-Kermani et al., "Vitamin A antagonizes decreased cell growth and elevated collagen-degrading matrix metalloproteinases and stimulates collagen accumulation in naturally aged human skin," *Journal of Investigative Dermatology*, vol. 114, no. 3, pp. 480–486, 2000.

[18] Y. Shao, T. He, G. J. Fisher, J. J. Voorhees, and T. Quan, "Molecular basis of retinol anti-ageing properties in naturally aged human skin in vivo," *International Journal of Cosmetic Science*, vol. 39, no. 1, pp. 56–65, 2017.

[19] E. A. Duell, S. Kang, J. T. Elder, J. J. Voorhees, and F. Derguini, "Extraction of human epidermis treated with retinol yields retro-retinoids in addition to free retinol and retinyl esters," *Journal of Investigative Dermatology*, vol. 107, no. 2, pp. 178–182, 1996.

[20] C. Piérard-Franchimont, D. Castelli, I. V. Cromphaut et al., "Tensile properties and contours of aging facial skin. A controlled double-blind comparative study of the effects of retinol, melibiose-lactose and their association," *Skin Research and Technology*, vol. 4, pp. 237–243, 1998.

[21] M. S. Chapman, "Vitamin a: history, current uses, and controversies," *Seminars in Cutaneous Medicine and Surgery*, vol. 31, no. 1, pp. 11–16, 2012.

[22] A. Wójcik, E. Bartnicka, P. Namieciński, and H. Rotsztejn, "Influence of the complex of retinol-vitamin C on skin surface lipids," *Journal of Cosmetic Dermatology*, vol. 14, no. 2, pp. 92–99, 2015.

[23] N. Sadick, B. L. Edison, G. John, K. L. Bohnert, and B. Green, "An advanced, physician-strength retinol peel improves signs of aging and acne across a range of skin types including melasma and skin of color," *Journal of Drugs in Dermatology*, vol. 18, no. 9, 2019.

[24] N. A. Dorgham, R. A. Hegazy, A. K. Sharobim, and D. A. Dorgham, "Efficacy and tolerability of chemical peeling as a single agent for melasma in dark-skinned patients: a systematic review and meta-analysis of comparative trials," *Journal of Cosmetic Dermatology*, vol. 19, no. 11, pp. 2812–2819, 2020.

[25] T. Gambichler, M. Skrygan, N. Tomi, S. Breuksch, P. Altmeyer, and A. Kreuter, "Significant downregulation of transforming growth factor-beta signal transducers in human skin following ultraviolet-A1 irradiation," *British Journal of Dermatology*, vol. 156, no. 5, pp. 951–956, 2007.

[26] T. Quan, T. He, S. Kang, J. J. Voorhees, and G. J. Fisher, "Solar ultraviolet irradiation reduces collagen in photoaged human skin by blocking transforming growth factor-beta type II receptor/Smad signaling," *American Journal Of Pathology*, vol. 165, no. 3, pp. 741–751, 2004.

[27] T. H. Quan, T. Y. He, S. Kang, J. J. Voorhees, and G. J. Fisher, "Ultraviolet irradiation alters transforming growth factor β/smad pathway in human skin in vivo," *Journal of Investigative Dermatology*, vol. 119, no. 2, pp. 499–506, 2002.

[28] H. Husein el Hadmed and R. F. Castillo, "Cosmeceuticals: peptides, proteins, and growth factors," *Journal of Cosmetic Dermatology*, vol. 15, no. 4, pp. 514–519, 2016.

[29] H. Sundaram, R. C. Mehta, J. A. Norine et al., "Topically applied physiologically balanced growth factors: a new paradigm of skin rejuvenation," *Journal of Drugs in Dermatology*, vol. 8, 2009.

[30] R. C. Mehta and R. E. Fitzpatrick, "Endogenous growth factors as cosmeceuticals," *Dermatologic Therapy*, vol. 20, no. 5, pp. 350–359, 2007.

[31] L. Rittié and G. J. Fisher, "Natural and sun-induced aging of human skin," *Cold Spring Harbor Perspectives in Medicine*, vol. 5, no. 1, 2015.

[32] M. Sun, P. Wang, D. Sachs et al., "Topical retinol Restores type I collagen production in photoaged Forearm skin within Four weeks," *Cosmetics*, vol. 3, no. 4, p. 35, 2016.

[33] K. Yoshimura, A. Momosawa, E. Aiba et al., "Clinical trial of bleaching treatment with 10% all-trans retinol gel," *Dermatologic Surgery*, vol. 29, no. 2, pp. 155–160, 2003.

[34] F. E. Cook-Bolden and S. F. Hamilton, "An open-label study of the efficacy and tolerability of microencapsulated hydroquinone 4% and retinol 0.15% with antioxidants for the treatment of hyperpigmentation," *Cutis*, vol. 81, 2008.

[35] P. E. Grimes, "A microsponge formulation of hydroquinone 4% and retinol 0.15% in the treatment of melasma and postinflammatory hyperpigmentation," *Cutis*, vol. 74, no. 6, 2004.

[36] D. Hexsel, R. Mazzuco, T. Dal'Forno, and D. Zechmeister, "Microdermabrasion followed by a 5% retinoid acid chemical peel vs. a 5% retinoid acid chemical peel for the treatment of photoaging-a pilot study," *Journal of Cosmetic Dermatology*, vol. 4, no. 2, pp. 111–116, 2005.