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The long term study of the difference in efficacy and effect rate of various concentrations of retinol (1500–6600 IU) in middle age women

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Abstract

Purpose

Retinol is widely used for topical application for antiaging. However, the efficacy and effect rate of different concentrations of retinol have been rarely analyzed. Therefore, in this study, the efficacy and rate of effect of retinol concentrations from 1500 IU to 6600 IU, on various skin parameters, have been compared.

Patients and methods

Seventy-two Korean women aged 40 to 59 years participated in this study. Retinol was used by them for 24 weeks; the effects were measured at 0, 2, 4, 8, 12, and 24 weeks. The measurement parameters for aging were crow's feet, forehead wrinkles, nasolabial fold, dermal density, and elasticity and that for skin color were skin brightness, yellowness, redness, and standard deviation of skin brightness. The texture of the skin was measured by measuring the skin roughness and pores, and the skin barrier function was evaluated through hydration, sebum, and desquamation.

Results

Low concentration retinol (1500–2500 IU) had a significantly higher effect in skin color, brightness, and elasticity and faster improvement rate in skin brightness and elasticity compared to that for high concentration (3300–6600 IU). High concentration of retinol had a significantly higher effect in wrinkles, dermal density and pores and faster improvement rate for wrinkles, skin texture, pores, and desquamation compared to that for low concentration.

Conclusion

This study evaluated the changes caused by different concentration of retinol over a long period of time. The results of this study have great implications as the optimal concentration of retinol can be prescribed for an accurate period for the desired results without side effects.

Introduction

Retinol is produced by hydrolysis of retinyl esters and can be oxidized into retinaldehyde, and then into retinoic acid. [1–3] The higher the activity of the metabolic pathways that convert retinyl esters to retinoic acid the higher the side effects. When such retinoids are topically applied, there are antiaging effects such as epidermal cells renewal, extracellular matrix production and melanocyte function modulation. [4–6] However, only the effects of retinoids at high concentrations (more than 0.4%) have been studied. In

addition, there are few studies that evaluate the difference in effect of retinoid according to its concentration, therefore, making it difficult to select the appropriate concentration for the optimal effect. Care has to be taken while using retinol at high concentration for a strong effect, as the risk of skin irritation is high. [7] A retinol concentration of more than 0.1% may cause irritation and inflammation due to the presence of epidermal growth factor receptor on the surface of the skin. This protein causes skin surface cells to proliferate. There have been reports of the skin turning pale and peeling off owing to the application of retinol-based cosmetics. [8] Therefore, it is difficult to prescribe a high concentration for improved efficacy owing to the side effects. According to the results of a study, which considered 0.1% of retinol as a relatively low concentration, fine wrinkle improved in week 12 of usage; however, the improvements before week 12 were not evaluated, making it difficult to ascertain when the fastest efficacy occurred. [9] However, the Ministry of Food and Drug Safety in Korea has granted permission for use of retinol in a concentration of 2500 IU (about 0.075%) for wrinkle improvement function, and many clinical reports on wrinkle improvement at 2500 IU compared to the control group are being reported. In addition to the wrinkle improvement function of retinol additional effects, such as skin color improvement and collagen production effect are known to occur with retinol use; however, the occurrence and the concentration of retinol which causes these effects are not known. [10,11] Therefore, in this study, we aimed to study the difference in efficacy and effect rate of different concentrations of retinol.

Material And Methods

Subjects and retinol samples application

Seventy-two Korean women aged 40 to 59 years, who voluntarily signed the consent form to participate in the study were included. They were divided into two groups of 36; Group 1 applied 1500 IU (approximately 0.045%) and 2500 IU (approximately 0.075%) of retinol on half of the face, and Group 2 applied 3300 IU (approximately 0.1%) and 6600 IU (approximately 0.2%) of retinol on half of their face. The measurement was done in a completely air-conditioned room equipped with humidity regulators. The ambient temperature was maintained at 22 ± 2°C and the relative humidity at 50 ± 5%. Participants stayed for 30 min in the laboratory before the clinical evaluation. There were seven measurement points, baseline, after 2 weeks, after 4 weeks, after 8 weeks, after 12 weeks, after 24 weeks. The study participants were asked to apply retinol every evening followed by sunscreen in the mornings. For more than 20 years, we have has stabilized retinol, which is vulnerable to heat, light, and oxygen, by using various capsulation technologies to protect retinol and control release to minimize side effects. And we recently developed a technology that delivers retinol more safely and effectively than ever before to the skin by perfectly stabilizing pure retinol itself in the product without having to capsulize it. This latest stabilization technology called Cube Cell™ isolates pure retinol in a mesh structure made up of polymer, a cocktail of antioxidants, and skin soothing ingredients, completely preventing the serial oxidation of retinol caused by heat, light, or oxygen. Also, by using Cube Cell™ technology, we've captured retinol of a much higher purity and content than before with much less side effects than previous retinol products, upgrading the effect and shelf-life (at least 24 months) of retinol by more than double the previous

products. Pregnant, lactating women, those with skin problems at the measuring site, and those receiving systemic steroids or light therapy within one month of participation were excluded from the study. Six participants were eliminated due to voluntary withdrawal of consent, and a total of 66 completed the experiment. The study was conducted following approval by the Institutional Review Board of Global Medical Research Center (certification number : GIRB-ETP-012-019). This study was conducted in accordance with the Declaration of Helsinki.

Measurement of skin aging

Skin wrinkles were measured once on both the left and right side at the test site (crow's feet, forehead, and nasolabial fold) using Antera 3D CS (Miravex, Ireland) equipment. This measuring instrument uses light-emitting diodes to measure the surface image of the skin, quantifying data extraction and skin conditions from the images utilizing the three-dimensional feature image of the embedded program. It means that as the wrinkle depth value decreases, skin wrinkles improve. The skin elasticity was measured using Cutometer Dual MPA 580 (courage khazaka electronic, Germany) on the cheeks once. Skin elasticity, the length of skin is pulled back into the probe using negative pressure the (450 mbar, 1.5 s off, 3 cycle) 2 mm diameter probe the infrared measurement. Elastic skin assessment indicator R2 the improved value is closer to the 1. Dermal density was measured using a Skin Scanner (Tpm, Germany) once on the test area crow's feet. The device measures the epidermal and dermal density using a 22 MHz ultrasonic transducer for measurement by generating an electric pulse, and the added values were used as a parameter. The measurement unit is %, and as such the dermal density improves as the measurement value increases.

Measurement of skin color

Skin color and skin color deviation were measured once using VISIA-CR (Canfield Science CO. Ltd, USA). Six constant locations were photographed using a high-resolution camera (Canon 5D, Japan) and a filter wheel, and a specific area (cheeks) was designated using an I-Max plus program (ver. 10.100.02.06, Korea) in the photographed image (Standard2 mode), and the skin color and color deviation values were analyzed and used as evaluation data.

Measurement of skin hydration, sebum, desquamation

The cheek skin hydration was measured by Corneometer CM825 (Courage & Khazaka, GmbH, Germany). This device measures the electrical reactive capacitance of skin. With increasing SC hydration, the electrical reactive capacitance increase. The skin sebum was measured by Sebumeter SM815 (Courage & Khazaka, GmbH, Germany) on the forehead. The measurement principal is the photometric method, the grease spot photometer. The corneocyte desquamation was harvested by adhesive-coated discs (D-SQUAME, Cuderm Corp. USA) from the cheeks. The specimen was collected by pressing once at a constant pressure using a D-squame pressure instrument. The samples were assessed by Visioscan VC98 (Courage khazaka electronic, Germany) a skin surface analyzer equipped with an ultraviolet A light source and a high-resolution video sensor chip. DI (desquamation Index) was used as an evaluation index; lower the measured DI (%) value, the better were the skin's dead cells.

Measurement of skin roughness and pores

For skin texture and pore measurement, the test area (cheeks) was measured using Antera 3D CS (Miravex, Ireland) equipment, and the average roughness (Ra) was used as evaluation data. It indicated that the skin texture improves as the skin roughness value decreases and as the average area measurement mm^2 of each pore decreases, skin pores are considered to improve.

Statistical analysis

Statistical evaluation was performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA). For the parametric test, repeated measures analysis of variance was used for data with normality assumption. Pairwise comparisons adjusted by the Bonferroni test were used for time comparisons. The comparison between groups was tested using multivariate analysis of covariance, and the data at week 0 was set as a covariate to confirm the significance as a parameter estimate. In order to compare the difference in the improvement rate for each retinol concentration, the slope was compared using the generalized estimating equation method. Statistical significance was determined at $p < 0.05$.

Results

Characteristics of test participants

There was no significant age difference between the two groups. Only women were recruited to eliminate bias due to differences in baseline skin characteristics according to sex. As for the skin type, more than 50% of the respondents analyzed their skin to be dry, and there was no significant difference between the two groups. In particular, no participant in either group believed that they had oily skin. In addition, more than 80% of the test participants answered that the skin was not sensitive; one participant dropped out of the study due to side effects in the group using 3300–6600 IU of retinol. Two participants in the low concentration (1500–2500 IU) and three in high concentration (3300–6600 IU) groups were eliminated at due to non-compliance. Therefore, finally 34 participants in the low concentration group and 32 participants in the high concentration group were included in the final test. More than 70% of the test participants were indoor workers, who were exposed to ultraviolet rays for a maximum of 1–2 h per day; hence, they were less likely to be exposed to ultraviolet radiation after using retinol. (Table 1.)

Table 1
Socio-demographic profile of participants

	1500–2500 IU	3300–6600 IU
	N (%)	N (%)
Age (years)		
30’s	-	-
40’s	19 (55.88)	16 (50.00)
50’s	15 (44.12)	16 (50.00)
Gender		
Female	34 (100)	32 (100)
Male	-	-
Skin Type		
Dry	17 (50.00)	18 (56.25)
Dehydrated and oily	3 (8.82)	4 (12.50)
Neutral	3 (8.82)	3 (9.38)
Oily	-	-
Combination	11 (32.35)	7 (21.88)
Sensitive skin		
Yes	1 (2.94)	5 (15.63)
No	33 (97.06)	27 (84.38)
Working environment		
Indoor	24 (70.59)	23 (71.88)
Outdoor	1 (2.94)	1 (3.13)
Mixed	9 (26.47)	8 (25.00)
Sun exposure time		
1 h	12 (35.29)	14 (43.75)
2 h	14 (41.18)	9 (28.13)
≥ 3 h	8 (23.5)	9 (28.13)

Effect of retinol on skin aging

Crow's feet significantly decreased from 2 to 24 weeks at all concentrations. The high-concentration retinol-using group showed significant improvement compared to the low-concentration retinol-using group at 2 weeks, thus, showing a rapid effect. However, the degree of improvement of crow's feet in 24-week was similar among individuals using retinol in concentrations between 1500 to 3300 IU, but the improvement was continuous, significant, and quick for those using 6600 IU of retinol. The group using 6,600 IU showed 11.56% improvement in crow's feet in the second week, whereas that using 1500 IU showed an improvement by 1.99%. The high concentration group showed improvement by 30% on average in the 24th week, but the low concentration improved only by 21% (Fig. 1. A). The forehead wrinkles significantly decreased from 2 weeks to 24 weeks at all concentrations however, they showed significant improvement in 2 weeks for participants using 6600 IU compared to those using 1500 IU. Significant improvement was seen from 12 to 24 weeks in group high compared to low concentration. The forehead wrinkles decreased by 1.49–2.41% in the second week at low concentration, and 11.95–13.83% at high concentration. At 24 weeks, the wrinkles decreased by 17.48% in the group using 1500 IU and by 26.60% in the group using 6600 IU (Fig. 1. B). The nasolabial fold significantly decreased from 2 weeks to 24 weeks at all concentrations compared to those using of 3300 IU of retinol, the nasolabial fold was significantly improved (2.82%) at 2 weeks in those using 1500 IU and (13.66%) at 24 weeks in those using 6600 IU. At week 24, those using 1500 IU showed an improvement by 18.78%, while those using 6600 IU showed an improvement by 31.08% (Fig. 1C). Dermal density showed significant improvement at all concentrations from 2 weeks to 24 weeks. However, it significantly improved from 2 weeks to 8 weeks by use of high concentrations compared to use of low concentrations. From 12 to 24 weeks, there was no significant difference at all concentrations; hence, the efficacy was the same. Dermal density improved by an average of 3% in the second week in those using low concentration but improved by an average of 7% in those using high concentration. In the 8th week, the group using low concentration showed an improvement by 9% on average, while the high concentration group showed an improvement by 11%, thus, gradually diminishing the difference in improvement (Fig. 1D). Skin elasticity (R2) significantly improved at all concentrations from 2 weeks to 24 weeks. However, those using 2500 IU compared to those using 6600 IU, showed significant improvement in the second week; at the 12th week, 1500 IU group showed significant improvement in elasticity compared to the high concentration group. At 24 weeks, there was no significant difference in all concentrations; hence, the efficacy was the same. R2 improvement averaged at 9% at 12 weeks for low concentration group, but only at 5% for high concentration group (Fig. 1E).

Effect of retinol on skin color improvement

Skin color brightness significantly improved from 2 weeks to 24 weeks at all concentrations. However, those using 1500 IU showed significant improvement from 2 weeks compared to those using 3300 and 6600 IU, and those using 2500 IU showed significant improvement compared to those using high concentration at 4 weeks. There was no significant difference in all concentrations at 8 to 24 weeks. In the fourth week of use of low concentrations, the average skin color became 2% brighter; however, that at

high concentrations became 0.5% brighter. Low concentrations initially showed rapid improvement in skin color (Fig. 2. A). At low concentrations, skin redness increased significantly from 2 weeks to 24 weeks, but there was no significant change at high concentrations. In addition, there was no difference in efficacy at each concentration (Fig. 2B). Usage of retinol at both low and high concentration decreased the skin yellowness significantly from 2 weeks to 24 weeks. The skin yellowness decreased significantly at 24 weeks by use of retinol at concentration of 3300 IU compared to other concentrations (Fig. 2C). Standard deviation of skin color brightness significantly decreased from 2 weeks to 24 weeks at all concentrations. A decrease in standard deviation of skin brightness indicates that the skin color has become uniform. However, there was no significant difference according to the concentration of retinol (Fig. 2D).

Effect of retinol on skin roughness and pore

Skin texture significantly improved from 2 weeks to 24 weeks at all concentrations. In the 12th week, the skin texture was significantly improved the high concentration than the low concentration. At 12 weeks of use, high concentration of retinol improved the skin texture by 25% on average, but low concentration improved it by 15%. However, there was no significant difference according to the concentration at the 24th week; hence, the effects of all concentrations were the same (Fig. 3A). At all concentrations, the pore area was significantly reduced from 2 weeks to 24 weeks of use. Particularly, the pore area was significantly improved at 2 weeks in those using high concentration of retinol than those using low concentration; use of retinol at 6600 IU significantly decreased the pore area from 8 weeks to 24 weeks compared to other concentrations (Fig. 3B).

Effect of retinol on skin barrier improvement

At all concentrations, skin moisture significantly improved from 2 weeks to 24 weeks. In particular, the hydration was significantly higher at 8 weeks and 12 weeks at the high concentration than at low concentration usage. In the 8th week of use, the high concentration of the skin hydration improved by 19%, but the low concentration of the skin hydration improved by 14%. There was no difference in hydration in all concentrations at 24 weeks (Fig. 4A). The sebum content decreased significantly at all concentrations from 2 to 24 weeks. At high concentration usage the sebum content decreased significantly from 2 to 24 weeks than low concentration usage. On the 24th week of use, the sebum content decreased by 46% on average at high concentration usage and by 23% at low concentration usage (Fig. 4B). The desquamation decreased significantly at all concentrations, but there was no significant difference according to the concentration (Fig. 4C).

Differences in improvement rates in aging parameters

There was a significant difference in the slope of wrinkle improvement at high concentration compared to that at low concentration in crow’s feet and nasolabial wrinkles; hence, the improvement rate was faster in high concentration. In terms of elasticity, low concentration were significantly faster to improve the effect than high concentraion. There was no difference in rate of improvement between 1500 and 2500 IU

for both wrinkle and elasticity, and between 3300 and 6600 IU. There was no difference in the rate of effect according to concentration in forehead wrinkles and dermal density (Table 2).

Table 2
Pairwise comparisons by generalized estimating equation analysis of aging parameters

Parameters	Group	B	SE	*p*-value
Crow's feet	1500–2500 IU	0.010	0.0425	-
	1500–3300 IU	**-1.070**	0.1741	< 0.001
	1500–6600 IU	**-1.274**	0.1935	< 0.001
	2500–3300 IU	**-1.080**	0.1727	< 0.001
	2500–6600 IU	**-1.284**	0.1921	< 0.001
	3300–6600 IU	-0.204	0.2558	-
Nasolabial fold	1500–2500 IU	0.014	0.0426	-
	1500–3300 IU	**-0.534**	0.1146	< 0.001
	1500–6600 IU	**-0.765**	0.1193	< 0.001
	2500–3300 IU	**-0.549**	0.1154	< 0.001
	2500–6600 IU	**-0.780**	0.1201	< 0.001
	3300–6600 IU	-0.231	0.1604	-
Elasticity	1500–2500 IU	0.043	0.0281	-
	1500–3300 IU	**-0.150**	0.0263	< 0.001
	1500–6600 IU	**-0.169**	0.0264	< 0.001
	2500–3300 IU	**-0.193**	0.0292	< 0.001
	2500–6600 IU	**-0.212**	0.0293	< 0.001
	3300–6600 IU	-0.019	0.0276	-
Notes: Crow's feet, Nasolabial fold (unit : μm), Elasticity (unit : X100 A.U)				
Abbreviation:				
B Beta,; SE, Standard error				

Differences in improvement rate in skin color

The brightening in skin color was significantly faster at low concentration usage than that at high concentration. In particular, 1500 IU usage showed the fastest improvement rate as deduced from the highest slope followed by 2500 IU, 3300 IU, and 6,600 IU usage. However, there was no significant difference between 1500 IU and 2500 IU and 3300 IU and 6600 IU. The standard deviation of skin brightness was significantly faster at 3300 IU and 6600 IU compared to 1500 IU and 2500 IU. There was no significant difference between 1500 IU and 2500 IU, 3300 IU and 6600 IU. When comparing the size of the slope, the effect was fastest to slowest in the order of 6600IU-3300IU-2500IU-1500IU usage (Table 3).

Table 3
Pairwise comparisons by generalized estimating equation analysis of skin color parameters

Parameters	Group	B	SE	*p*-value
Skin brightness	1500–2500 IU	-0.016	0.0236	-
	1500–3300 IU	**-0.063**	0.0202	< 0.01
	1500–6600 IU	**-0.056**	0.0205	< 0.01
	2500–3300 IU	**-0.048**	0.0200	< 0.05
	2500–6600 IU	**-0.040**	0.0203	< 0.05
	3300–6600 IU	0.007	0.0162	-
Skin redness	1500–2500 IU	-0.013	0.0160	-
	1500–3300 IU	**-0.037**	0.0167	< 0.05
	1500–6600 IU	**-0.034**	0.0157	< 0.05
	2500–3300 IU	**-0.024**	0.0183	-
	2500–6600 IU	**0.021**	0.0174	-
	3300–6600 IU	0.003	0.0180	-
SD of Skin brightness	1500–2500 IU	-0.002	0.0057	-
	1500–3300 IU	**-0.032**	0.0063	< 0.001
	1500–6600 IU	**-0.037**	0.0071	< 0.001
	2500–3300 IU	**-0.029**	0.0057	< 0.001
	2500–6600 IU	**-0.034**	0.0065	< 0.001
	3300–6600 IU	-0.005	0.0070	--
Notes: Skin brightness, Skin redness, SD of skin brightness (unit : A.U)				
Abbreviation: B Beta,; SE, Standard error, : SD, Standard deviation				

Differences in improvement rate in skin roughness and pore

Skin texture improved significantly faster at high concentration usage compared to low concentration usage. There was no significant difference in improvement speed between 1500 IU and 2500 IU, 3300 IU and 6600 IU. When comparing the size of the slope, the improvement speed was fastest to slowest in the order of 3300 IU-6600 IU-2500 IU-1500 IU. The pore area decreased significantly faster at high concentration usage compared to a low concentration usage. There was no difference in improvement rate between 1500 IU and 2500 IU, 3300 IU and 6600 IU. When comparing the size of the slope, the improvement speed was fastest to slowest in the order of 3300IU-6600IU-1500IU-2500IU (Table 4).

Table 4
Pairwise comparisons by generalized estimating equation analysis of skin roughness and pore

Parameters	Group	B	SE	*p*-value
Skin roughness	1500–2500 IU	-0.001	0.0086	-
	1500–3300 IU	**-0.056**	0.0098	< 0.001
	1500–6600 IU	**-0.040**	0.0098	< 0.001
	2500–3300 IU	**-0.054**	0.0088	< 0.001
	2500–6600 IU	**-0.039**	0.0088	< 0.001
	3300–6600 IU	0.015	0.0100	-
Skin pore	1500–2500 IU	0.082	0.1485	-
	1500–3300 IU	**-0.845**	0.1616	< 0.001
	1500–6600 IU	**-0.712**	0.1669	< 0.001
	2500–3300 IU	**-0.927**	0.1554	< 0.001
	2500–6600 IU	**-0.794**	0.1610	< 0.001
	3300–6600 IU	0.133	0.1731	-
Notes: Skin roughness, Skin pore (unit : mm)				
Abbreviation: B Beta,; SE, Standard error,				

Differences in improvement rate in skin barrier

The improvement rate of sebum content was significantly faster at high concentration usage compared to low concentration usage. There was no significant difference in improvement speed between 1500 IU

and 2500 IU, and between 3300 IU and 6600 IU. When comparing the size of the slope, the effect was the fastest to slowest in the order of 6600IU-3300IU-1500IU-2500IU. The improvement rate of desquamation was significantly faster when used at high concentrations compared to when used at low concentrations. There was no significant difference in improvement speed between 1500 IU and 2500 IU, and between 3300 IU and 6600 IU. When comparing the size of the slope, the effect was fastest to slowest in the order of 3300IU-6600IU-2500IU-1500IU. There was no significant difference in effect rate of hydration content of according to concentration (Table 5).

Table 5
Pairwise comparisons by generalized estimating equation analysis of skin barrier parameters

Parameters	Group	B	SE	*p*-value
Sebum	1500–2500 IU	-0.114	0.2436	-
	1500–3300 IU	**0.905**	0.3133	< 0.01
	1500–6600 IU	**0.945**	0.3048	< 0.01
	2500–3300 IU	**1.019**	0.3105	< 0.01
	2500–6600 IU	**1.060**	0.3019	< 0.001
	3300–6600 IU	0.041	0.3605	-
Skin Desquamation	1500–2500 IU	-0.015	0.0162	-
	1500–3300 IU	**-0.117**	0.0140	< 0.001
	1500–6600 IU	**-0.101**	0.0129	< 0.001
	2500–3300 IU	**-0.101**	0.0145	< 0.001
	2500–6600 IU	**-0.085**	0.0135	< 0.001
	3300–6600 IU	0.016	0.0108	-
Notes: Sebum (unit : μg/cm^2), Skin desquamation (unit :%)				
Abbreviation: B Beta,; SE, Standard error,				

Discussion

It is a widely known fact that retinol is effective in skin aging. In this study, the efficacy of high and low concentrations of retinol for most skin indicators was distinguished. In particular, high concentrations of retinol had better efficacy for improving wrinkles, dermal density, pores, and hydration than low concentrations whereas low concentrations of retinol had higher efficacy in correcting skin color and elasticity than high concentrations. Moreover, this study also evaluated the rate of the effect, by comparing large changes that occurred over the entire 24-week period and not small changes that

occurred every week. Knowing the efficacy and rate of effect of retinol at various concentrations is important as optimal concentrations can be used to resolve particular skin problems. Care should be needed precisely while using high concentrations of retinol as it can cause irritation to the skin, but if used for the right purpose for an optimal time, side effects can be reduced and the beneficial effect can be maximized. In addition, for improving dermal density, elasticity, brightness, texture, and hydration people with sensitive skin can use low concentration retinol for 24 weeks as retinol at all concentrations have the same effect on these parameters when used for a long time. Conversely, for wrinkles, dermal density and pores, high concentrations for a short period can be used as they can be improved without long-term use. When retinol of high concentration is applied topically, dermal extracellular matrix increases, resulting in thickening of the dermis by increased collagen production. [12] Therefore, at high concentrations retinol was also effective for deep wrinkles (forehead wrinkles and nasolabial fold) and improved the density of the dermis. The increase in skin redness at low concentrations could indicate an improvement in the color of the skin and not skin irritation. A study that evaluated the face value of 160 Korean women, reported an average of redness of 15.79 a.u. for women in their 40's and 17.25 a.u. for women in their 50's [13]; however, in this study, the average cheek redness was 9.16 a.u. This result could be attributed to the fact that more than 70% of the participants were indoor workers and the amount of ultraviolet rays exposure per day was less than 2 h. Low skin redness is considered to be a cognitively unhealthy skin color, and studies have shown that the skin is perceived to look healthy when the skin color L* and a* values increases. [14] Unlike most of the test participants who believed their skin to be dry, the average amount of skin hydration was low at 55 a.u in the actual skin measurement, but the amount of sebum was high at 150 μg/cm^2 on average. Skins that feel dry but look oily lacks hydration. This type of skin is called dehydrated oily skin. Skin care, which increases hydration content and decreases sebum content such as, high concentration of retinol is important for these skin. However, test participants in their 40's and 50's perceived their skin to be dry due to age, and excessive sebum removal in them can make their skin feel drier; hence skin with low sebum content can use low-concentration of retinol to adjust the oil and water balance. In particular, studies have shown that dehydrated and oily skin has high Trans-epidermal water loss(TEWL), rough skin texture, and dark skin color. [15] Hence, the use of low concentration of retinol for a long time, similar to usage of high concentration of retinol can be helpful in such cases because it improves skin color quickly and improves skin texture This study, had a limitation as it only included small number of Korean women of limited age range to reduce the deviation. In future studies, we intend to study retinol efficacy in men, skin changes caused by retinol in young age, and differences in efficacy and rate of effect of retinol in various ethic skin.

Declarations

Disclosure

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Data Availability

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Figures

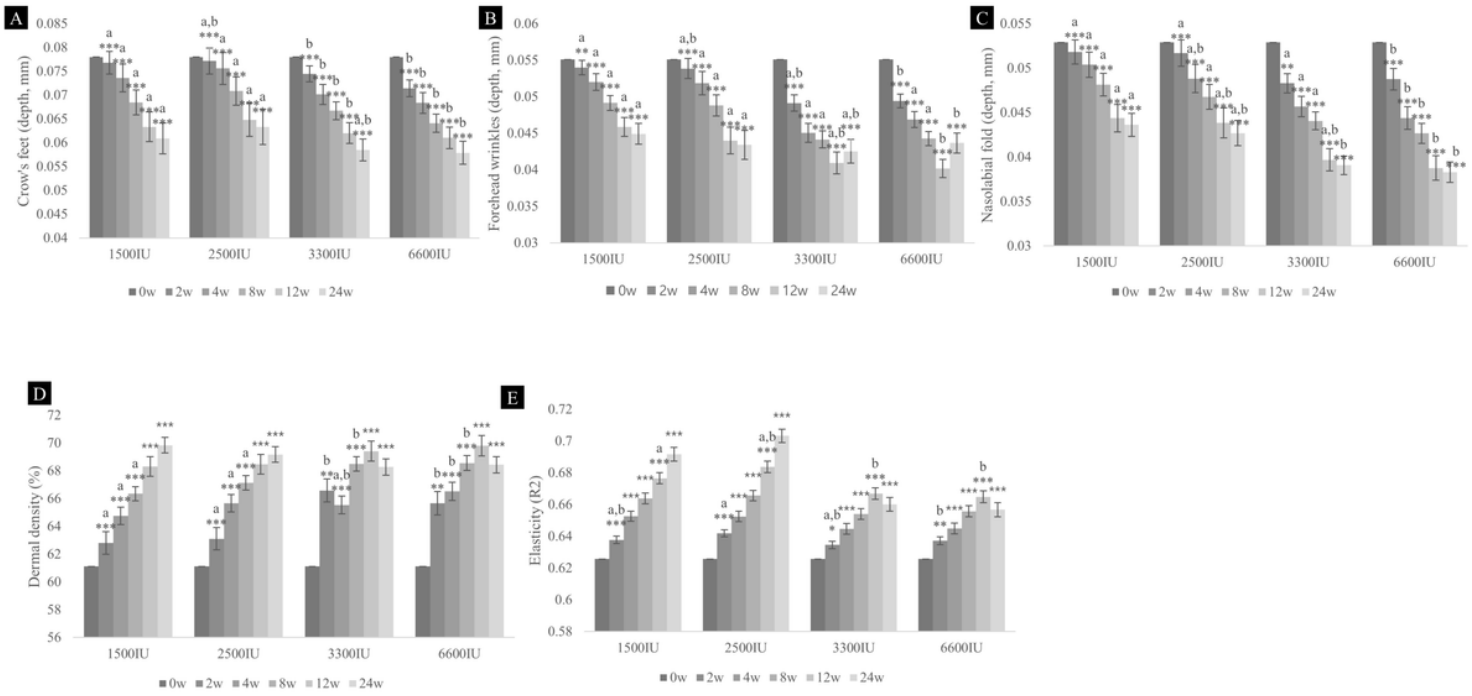

Figure 1

Antiaging effects of various retinol concentrations

Effects on crow's feet (a), forehead wrinkles (b), nasolabial fold (c), dermal density (d) and elasticity (e) after use of retinol from 1500 IU to 6600 IU during 0 to 24 weeks. Changing effect according to time, repeated measure analysis of variance. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, Changes over time between groups, multivariate analysis of covariance, Mark in different characters if there are differences. A statistically significant difference was verified as $p < 0.05$. 0 w, baseline; 2 w, after 2 weeks; 4 w, after 4 weeks; 8 w, after 8 weeks; 12 w, after 12 weeks; 24 w, after 24 weeks

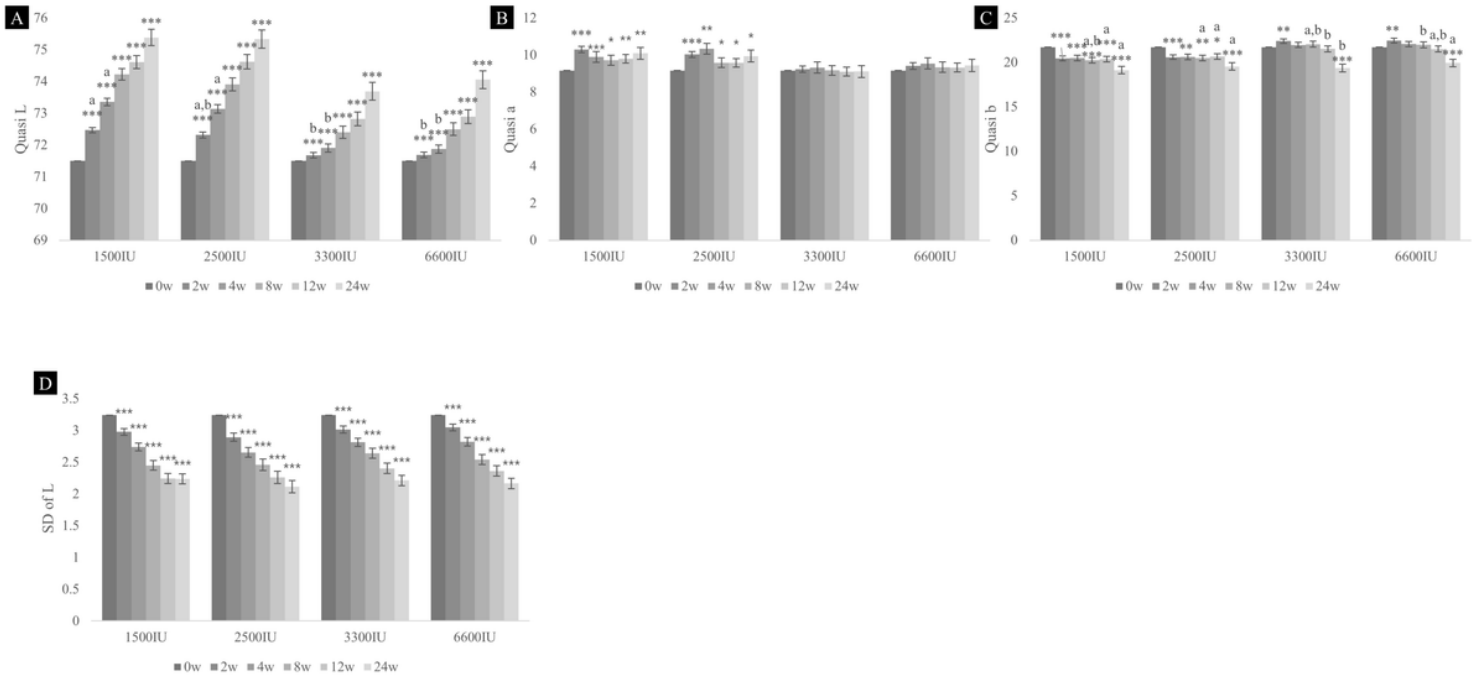

Figure 2

Brightening effects of various retinol concentrations

Effects on skin brightness (Quasi L) (a), skin redness (Quasi a) (b), skin yellowness (Quasi b) (c) and standard deviation of skin brightness (d) after use of retinol from 1500 IU to 6600 IU during 0 to 24 weeks. Changing effect according to time, repeated measure analysis of variance. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, Changes over time between groups, multivariate analysis of covariance, Mark in different characters if there are differences. A statistically significant difference was verified as $p < 0.05$. 0 w, baseline; 2 w, after 2 weeks; 4 w, after 4 weeks; 8 w, after 8 weeks; 12 w, after 12 weeks; 24 w, after 24 weeks

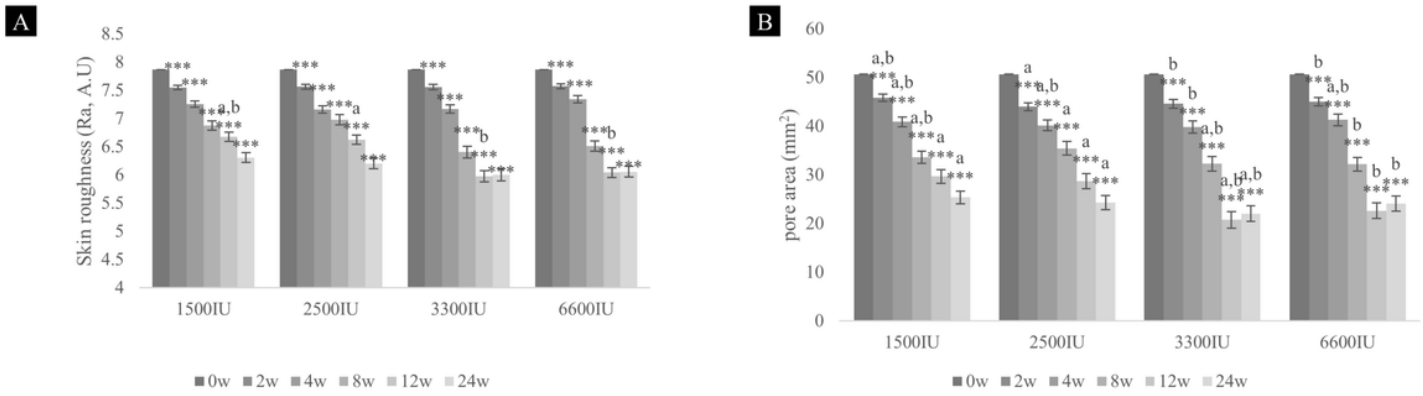

Figure 3

Skin roughness and pore effect of various retinol concentrations

Effects of skin roughness (Ra) (a) and skin pore (b) after use of retinol from 1500 IU to 6600 IU during 0 to 24 weeks. Changing effect according to time, repeated measure analysis of variance. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, Changes over time between groups, multivariate analysis of covariance, Mark in different characters if there are differences. A statistically significant difference was verified as $p < 0.05$. 0w, baseline; 2 w, after 2 weeks; 4 w, after 4 weeks; 8 w, after 8 weeks; 12 w, after 12 weeks; 24 w, after 24 weeks

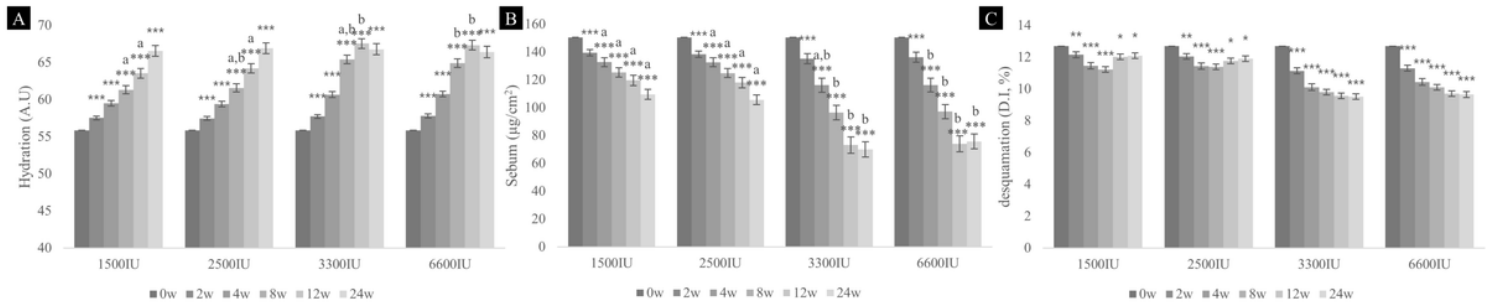

Figure 4

Skin surface changes according to various retinol concentrations

Effects of skin hydration (a), sebum (b) and desquamation (c) after use of retinol from 1500 IU to 6600 IU during 0 to 24 weeks. Changing effect according to time, repeated measure analysis of variance. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, Changes over time between groups, multivariate analysis of covariance, Mark in different characters if there are differences. A statistically significant difference was verified as $p < 0.05$. 0 w, baseline; 2 w, after 2 weeks; 4 w, after 4 weeks; 8 w, after 8 weeks; 12 w, after 12 weeks; 24 w, after 24 weeks