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Efficacy of Topical 0.05% Retinaldehyde in Skin Aging by Ultrasound and Rheological Techniques

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Key Words

Retinaldehyde · Photoaging · Echography · Elasticity · Stiffness · Skin thickness

Abstract

Background: The natural precursor of retinoic acid, i.e. retinaldehyde, has been proven to exert retinoid activities. ***Aim and Methods:*** The aim of this prospective instrument study was to determine the effect of topical retinaldehyde 0.05% on the physical properties of aging skin. This was performed using two devices, namely a high-resolution (70–80 μm) ultrasound scanner, which visualizes the thickness of both the epidermis and the dermis, and an echorheometer, which assesses the stiffness and elasticity of the skin by suction. In a 1-year study, 21 patients applied retinaldehyde cream 0.05% on the face, while another group of 19 volunteers were only treated with an emollient (control group). Epidermal and dermal thicknesses were measured on the forehead and temple, and stiffness and elasticity were measured on the forehead only. All the instrumental parameters were assessed at baseline and at the end of treatment. ***Results:*** Compared to the control group, retinaldehyde treatment induced a significant increase in epidermal thickness of the temple, as well as in cutaneous elasticity ($p < 0.01$). Similarly, retinaldehyde treatment tended to increase dermal thickness and reduce cutaneous stiffness, but no statistical difference could be observed between the two groups. ***Conclusion:*** Taken together, the results further suggest that retinaldehyde has counteracting effects on skin aging.

Introduction

Chronological skin aging and chronic exposure to sunlight induce skin changes that are probably interrelated [1]. These include skin atrophy [2], reduction of elasticity [3] and an increase in cutaneous stiffness [4, 5]. These alterations result in clinical modifications of the skin, including wrinkling, color changes (yellowing, uneven pigmentation) and laxity of the skin.

Topical retinoic acid was the first substance which associates clinical improvement of skin appearance with histological changes [1, 6]. In a recent clinical trial, the natural precursor of retinoic acid, retinaldehyde, has also been proven to be effective in the reduction of facial wrinkles [7]. The aim of this prospective instrumental study was to evaluate the effects of topical retinaldehyde on skin aging and photoaging, using noninvasive techniques such as cutaneous echography and echorheometry.

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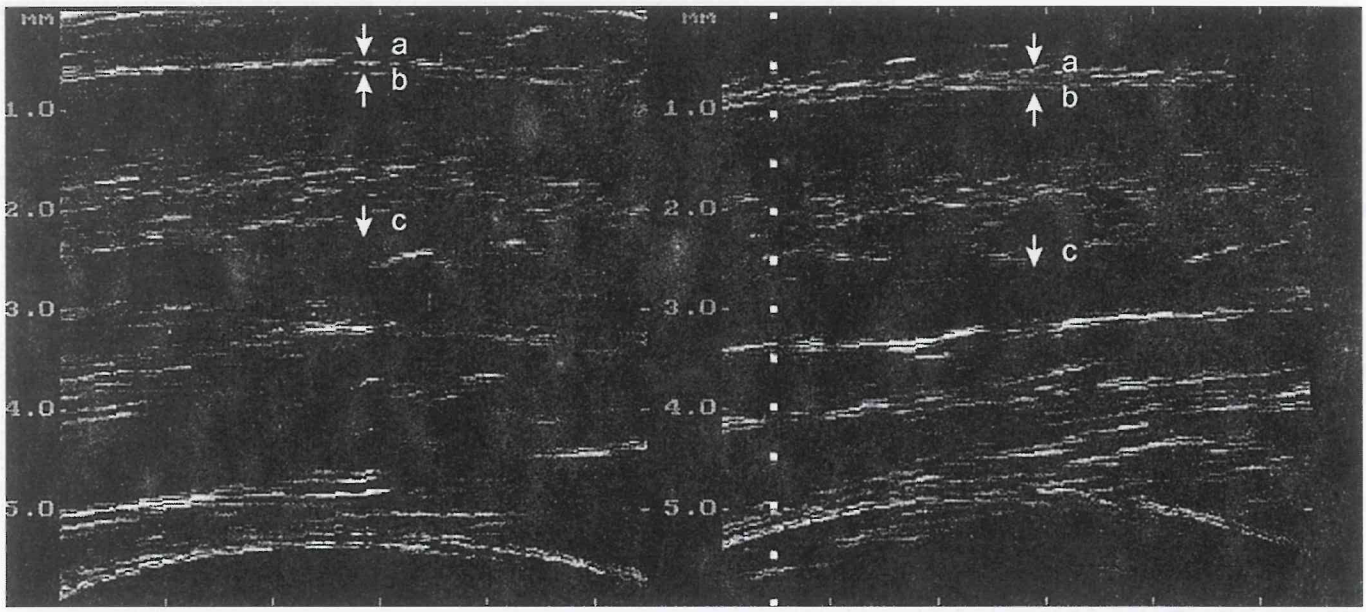

A B

Fig. 1. A typical example of the modulation of retinaldehyde 0.05% before (**A**) and after (**B**) the 1-year treatment on the temple, using a 20-MHz ultrasound technique. Three echobands were observed: a = the gel-stratum corneum interface, b = the epidermis-dermis interface and c = the dermis-hypodermis interface. **A** Epidermis = 110 μm; dermis = 1.42 mm. **B** Epidermis = 130 μm; dermis = 1.58 mm.

Table 1. Demographic data and baseline values of the physical parameters in the study population (n = 40)

	Retinaldehyde	Control
Patients, n	21	19
Age, years	47.4 ± 4.93	47.1 ± 5.47
Weight, kg	53.9 ± 4.2	56.5 ± 6.0
Height, cm	160.3 ± 3.1	160 ± 4.5
Type of skin, n		
Dry	9	6
Normal/mixed	12	11
Greasy	0	2
Instrumental values		
Forehead epidermis thickness, μm	96 ± 4	98 ± 5
Temple epidermis thickness, μm	106 ± 3	97 ± 4
Forehead dermis thickness, mm	1.4 ± 0.05	1.58 ± 0.05
Temple dermis thickness, mm	1.24 ± 0.05	1.41 ± 0.05
Elasticity index, arbitrary units	0.35 ± 0.01	0.32 ± 0.01
Stiffness, kPa	218 ± 20	220 ± 19

Results are expressed as means ± SEM.

Methods

The study population comprised women over 35 years of age, with moderate to severe photodamage. Patients applied either retinaldehyde 0.05% on their faces once daily for 1 year, or were left untreated (emollient only, control group). None of the patients had applied topical retinoids on the treatment areas for more than 4 weeks during the 6-month period before the initiation of the study treatment. None had used chemical peels, exfoliants or any abrasive substance on the face within 45 days before entry into the study. Pregnant and nursing women and patients who planned to use PUVA for tanning were excluded, as well as those with suspected skin cancer or any other con-

dition that could interfere with their evaluation. This study was performed from January 1996 to January 1997. Patients were seen every 3 months for tolerance assessment and product supply.

Instrumental evaluation was performed at baseline and at the end of treatment (1 year). For evaluation visits, patients were asked not to apply any topical product on the face the night before. The test sites (forehead and temple) were precisely located using a transparent plastic film that was positioned according to skin features (moles, hair line and eyebrows). Thicknesses of the dermis and epidermis on the temple and the forehead were measured using a high-resolution B mode 20-MHz ultrasonic device (DermCup 2020®, 2MT, Toulouse, France) [8, 9]. The resolution of the apparatus (axial 70–80 μm, lateral 200–300 μm) allowed observance of the two echos from the gel-stratum corneum and epidermis-dermis interfaces, as shown in figure 1. Thus, the assessment of the epidermal and the dermal thicknesses was made possible by the measurements of the length (μm) between the echos. Stiffness and elasticity of the skin on the forehead were evaluated using an echorheometer, i.e. combining the ultrasound technique (20 MHz) and a deformation system under standard suction conditions. The echorheometer allowed measurement of the kinetics of vertical displacement of the skin under suction. From this kinetics profile, two independent parameters were determined: (i) the stiffness which is Young's modulus, as a reflectance of the resistance of the skin to the suction; (ii) the elasticity index, calculated by an algorithm which reflects the skin recovery of its initial state after suction. These two parameters, which describe the intrinsic mechanical properties of the skin, are independent of its thickness. Full details of the technique and of the mechanical parameters are described elsewhere [9–11]. For each measurement, the relative humidity (mean ± SD: 39 ± 7%) and temperature (23 ± 2 °C) of the room were standardized. All measurements were made by the same investigator.

Results of the study parameters were expressed as means ± SEM. Changes from baseline were analyzed using Student's test and the Wilcoxon test, according to the normal and nonnormal distribution of the values, respectively. Differences between the retinaldehyde and the control group were analyzed using the Bonferroni test.

Results

A total of 44 women were enrolled in the study. Among the enrolled population, 4 patients were excluded from the study, because they applied nonpermitted products (α-hydroxy acids or retinoic acid). No patient was withdrawn from the study because of adverse events. Accordingly, 40 patients, with 21 patients in the retinaldehyde group and 19 in the control group, constituted the standard analysis population. At baseline, the two study groups were found to be comparable in their demographics and instrumental values (table 1).

Changes from baseline of the instrumental parameters after 1 year (end of treatment) are illustrated in figures 2–5. Globally, epidermal thickness on the forehead was increased in the retinaldehyde group by about 10% ($p = 0.005$) and in the control group by about 4% (nonsignificant, fig. 2).

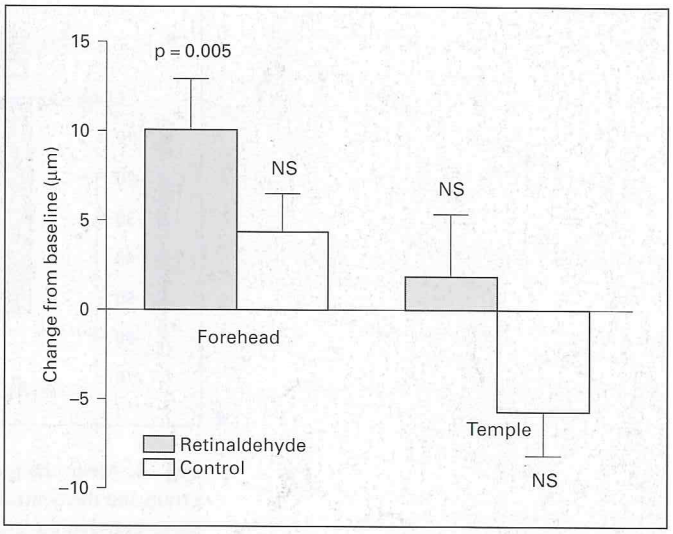

Fig. 2. Mean changes from baseline of epidermal thickness (± SEM) on the forehead and the temple, in the retinaldehyde group and the control group. For the intragroup analysis, p values are represented in the graph. For the intergroup analysis, only a statistically significant difference in favor of retinaldehyde was observed on the temple ($p < 0.01$).

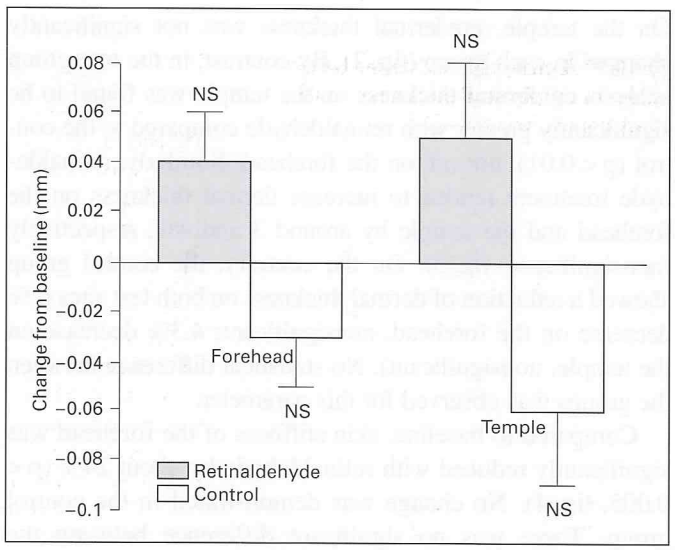

Fig. 3. Mean changes from baseline of dermal thickness (± SEM) on the forehead and the temple, in the retinaldehyde group and the control group. For the intragroup analysis, p values are represented in the graph. For the intergroup analysis, no statistically significant difference was observed at both sites.

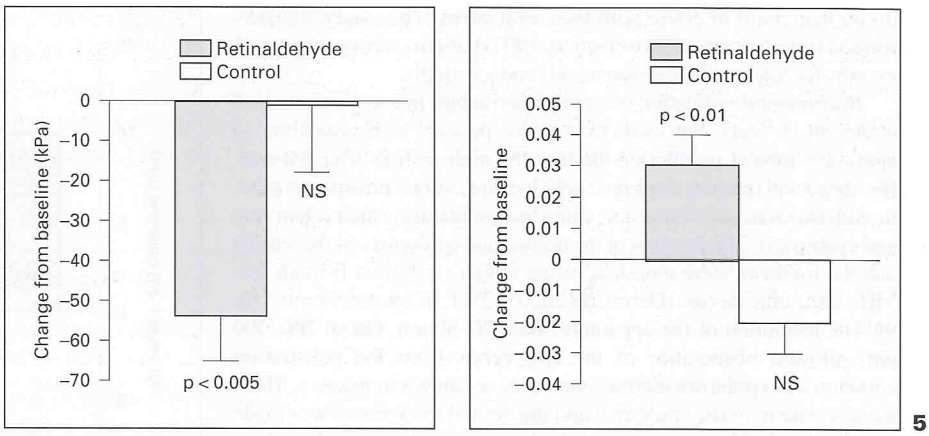

Fig. 4. Mean changes from baseline of stiffness (± SEM) on the forehead, in the retinaldehyde group and the control group. For the intragroup analysis (comparison to baseline), p values are represented in the graph. For the intergroup analysis, no statistically significant difference was observed.

Fig. 5. Mean changes from baseline of elasticity (± SEM) on the forehead, in the retinaldehyde group and the control group. For the intragroup analysis (comparison to baseline), p values are represented in the graph. For the intergroup analysis, a significant difference in favor of retinaldehyde was observed ($p < 0.01$).

On the temple, epidermal thickness was not significantly changed in each group (fig. 2). By contrast, in the intergroup analysis epidermal thickness on the temple was found to be significantly greater with retinaldehyde compared to the control ($p < 0.01$), but not on the forehead. Similarly, retinaldehyde treatment tended to increase dermal thickness on the forehead and the temple by around 3 and 4%, respectively (nonsignificant, fig. 3). On the contrary, the control group showed a reduction of dermal thickness on both test sites (2% decrease on the forehead, nonsignificant; 4.3% decrease on the temple, nonsignificant). No statistical difference between the groups was observed for this parameter.

Compared to baseline, skin stiffness of the forehead was significantly reduced with retinaldehyde by about 24% ($p < 0.005$, fig. 4). No change was demonstrated in the control group. There was no significant difference between the groups. Similarly, skin elasticity was enhanced with retinaldehyde by about 4% ($p < 0.01$, fig. 5), whereas it tended to be decreased in the control group (3% decrease, nonsignificant). A statistically significant difference between the groups was here achieved ($p < 0.01$).

Local tolerance was shown to be good in all patients. Indeed, only transitory scaling and/or erythema of mild severity were reported in 2 patients of the retinaldehyde group, within the first 3 months of treatment, and no patient of the control group. Consequently, no interference between the instrumental values and the tolerance results could be considered.

Discussion

Our results indicate that retinaldehyde is able to reverse some physical alterations involved in skin aging and photoaging. Its effects were more pronounced on epidermal thickness and cutaneous elasticity than on dermal thickness and skin stiffness, all four of these being the hallmarks of the skin aging process.

Instrumental investigation of the physical properties of the skin allows the study of its physiological and pathological characteristics [12, 13]. For instance, B mode high-resolution ultrasound was demonstrated to be a rapid and sensitive tool for measuring skin thickness. Its validation and reproducibility were confirmed by parallel measurements of this latter using the histological technique [14, 15]. Similarly, the echorheometer technique was validated in-house on elastic membrane models, the mechanical properties of which had previously been calibrated [9]. Its accuracy and reproducibility were found to be satisfactory [10]. Accordingly, these two techniques appeared to be valuable systems for measuring mechanical properties of the skin.

According to the literature, epidermal and dermal thicknesses [2, 16, 17] as well as elasticity of the skin decrease progressively during the long-term aging process [3], whereas skin stiffness increases [4, 18]. Globally, our data further confirm the literature, as shown in our control group. By contrast, retinaldehyde 0.05% appears to counteract the physical characteristics observed in skin aging and photoaging. In this study, because the mechanical parameters stiffness and elasticity were shown to be independent of the cutaneous thickness, it is likely that the beneficial effects of retinaldehyde are due to some recovery in the quality or density of the structures that are involved in skin suppleness and elasticity (e.g. collagen and elastic fiber network) rather than to its effect on skin thickness only. Taken together, the results confirm that retinaldehyde has restorative effects on skin aging and photoaging.

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