Cutaneous absorption of retinyl palmitate and acetate in healthy volunteers

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Introduction

Vitamin A derivatives (retinoids) have been demonstrated to stabilize cutaneous free radicals. Retinoids have subsequently been used in reduction of cutaneous photo aging and photocarcinogenisis. Retinoic acid has been related to decreased epidermal hyperplasia, to increased dermal collagen content, and to decreased collagenase activity. Compliance to daily use of topically applied retinoic acid is however, decreased by side effects: burning and stinging sensation, development of erythema and papules.

Therapeutic use of retinyl esters has been hampered by lack of cutaneous absorption. The development of percutaneous drug delivery by liposomes has however, offered new possibilities.

The aim was to investigate cutaneous absorption of the esters retinyls palmitate and retinyl acetate from topical repetitive cream application.

Material and methods

Fifteen healthy women, age (45 ±2.1)(mean ±SD) years participated in the present investigation. Retinyl cream (Beauté Pacifique, Denmark) (0.3 ml) with 10.000 IU retinyl/g, 60% retinyl palmitate and 40% retinyl acetate, or placebo cream were applied to a skin area of 36 cm^2 of the medical side of the upper arms once daily in five consecutive days.

The creams were applied placebo-controlled, double-blinded and randomized. High frequency ultrasound (20 MHz) examination of the skin was performed prior to and after skin application period.

Side effects as stinging, burning, redness and scaling were scored from 0 (none) to 3 (severe).

Suctions blisters from all treated skin areas were made and the blister fluids were by High Performance Liquid Chromatography (HPLC) analyzed for concentrations of retinyl palmitate, retinyl acetate and retinol.

Results

From sonographic skin examination no significant difference in thickness of epidermal entrance echo, thickness of dermal echo or of total skin thickness were demonstrated.

However, a significant percent increase in mean dermal sonographic density from the skin treated with retinyl cream (25.2% ±24.8%)(mean ±SD) compared to placebo cream (10.4% ±22.2%) was demonstrated. No significant percent change in low-echogenic density between skin treated with retinyl cream and placebo cream was demonstrated.

Compared to the placebo treated skin the retinol co0ncentration (247.4 ± 89.4 ng/ml)(mean ±SD) and the retinyl palmitate concentrations (7.0 ± 8.6 ng/ml) were both significantly higher in the suction blister fluid from the skin treated with retinyl containing cream ($p<0.05$).

The retinyl acetate concentration in the blister fluid was not significantly different between the skin applied with cream containing retinyl compared to the placebo treated skin.

One subject initially experienced minimal itch (score 1) at the area treated with active cream. No subjects developed erythema of the skin.

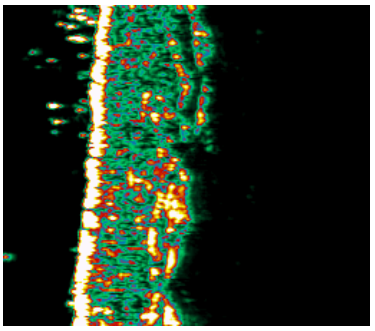

Figure 1.
Sonographic picture (subject 01) before application of retinyl cream. Superficially is the high-echogenic epidermal entrance echo, below is the dermal echo of lower echogenicity. Most profound is the subcutaneous layer with absent echo.

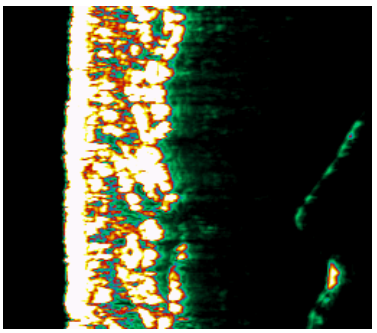

Figure 2
Sonographic picture (subject 01) after application period of retinyl cream. The dermal echo demonstrates increased markedly echogenicity.

Conclusion

The sonographic skin measurement demonstrates an increased dermal density without change in low-echogenic density, i.e. water content. This may reflect either increased cellularity or increased fiber content. The present data demonstrates a cutaneous uptake of retinyl

References

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