

# TOPICAL TRETINOIN FOR PHOTOAGING. THE CHINA EXPERIENCE.

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## Synopsis

Topical tretinoin (Retin-A®, Ortho Pharmaceuticals) was applied for 6-9 months to photoaged faces of 27 Chinese, mostly women, living in North China where climatic conditions are very unfavorable. Summers are hot and sunny, predisposing to photodamage. The weather is also frequently dry and windy predisposing to dryness.

The results were similar to those previously described on Orientals in Thailand, Phillipines and S.E. Asia. Based on global estimates, most subjects showed a satisfactory degree of improvement in over-all appearance.

Beneficial effects were noteworthy for the following features.

- 1) Dyspigmentation:** Hyper-pigmented spots and blotches faded. Skin color became more uniform.
- 2) Wrinkles:** Fine wrinkles, especially those around the eyes, were effaced.
- 3) Sallowiness:** Yellow-tinged skin was replaced by a rosy glow, which added greatly to attractiveness.
- 4) Dry-roughness:** The surface became smoother and less scaly.

A control group treated with a moisturizer.

Moisturizer failed to show appreciable benefits in any of the above features.

Irritant reactions, consisting mainly of burning, scaling and erythema were more common than in Caucasoids. Almost a third of the participants dropped out because of these adverse changes.

This experience corresponds to a widespread belief by physicians that Oriental skin is more "sensitive" to potentially irritating substances.

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## Riassunto

La tretinoina topica (Retin-A®, Ortho Pharmaceuticals) è stata applicata per 6-9 mesi al volto di 27 cinesi, principalmente donne, affette da foto-invecchiamento e provenienti dal Nord della Cina dove le condizioni climatiche sono molto sfavorevoli.

I risultati sono simili a quelli descritti in precedenza per gli orientali della Thailandia, delle Filippine e del Sud/Est Asiatico. Al controllo la maggior parte dei soggetti ha mostrato un soddisfacente grado di miglioramento sull'apparenza globale, dopo un controllo di tutti i parametri presi in considerazione. Effetti migliorativi si sono verificati nei seguenti parametri:

- (1) Depigmentazione:** nelle zone cutanee iperpigmentate il colore delle cute è divenuto più uniforme.
- (2) Rughe:** le rughe sottili si sono ridotte soprattutto nella zona del contorno occhi.

(3) **Colorito giallastro:** le aree cutanee di aspetto giallastro sono state sostituite da aree rosate che hanno migliorato notevolmente il grado di attrazione individuale.

(4) **Secchezza-rugosità:** la superficie cutanea è diventata più liscia e meno rugosa. Un gruppo di controllo trattato con un'idratante non medicata non ha mostrato apprezzabili miglioramenti sui parametri descritti.

Le reazioni irritative, quali l'arrossamento evidente e le fessurazioni cutanee, sono state più comuni rispetto ai Caucasici.

Quasi un terzo dei partecipanti hanno interrotto il trattamento a causa di questi effetti collaterali. Questa esperienza convalida quanto sostenuto dai medici che la cute degli orientali è più "sensibile" a sostanze potenzialmente irritanti.

## INTRODUCTION

Numerous reports all over the world have documented the beneficial effects of topical vitamin A acid (tretinoin) in improving the appearance of photodamaged skin (1,2,3,4).

Clinically, fine wrinkles become effaced, dyspigmentations fade, the rough-dry surface becomes smoother, laxity gives way to firmer more elastic skin, uneven texture becomes uniform, yellow sallowness is replaced by a rosy glow. The over-all effect is toward a more youthful and more physically attractive skin.

Histologically, epidermal atrophy and atypia are completely corrected accompanied by a normal pattern of differentiation. Keratinocytes become hypertrophic with evidence of increased metabolic activity, associated with an increase in epidermal turnovers, dense clusters of hyper-melanized pigment granules become dispersed and individual melanosomes contain much less melanin. New collagen is laid down sub-epidermally and new small vessels are generated (angiogenesis) (5,6,7). Physiologic and immunologic functions are also enhanced.

## PHOTOAGING IN ORIENTALS

Reports from Thailand, the Phillipines and Asia have demonstrated that the capacity of tretinoin to reverse the clinical and histologic signs of photo-damage in Oriental skin is similar to that of Caucasoids (7,8,9,10).

In Orientals, dyspigmentations and uneven texture are not only more frequent than in Caucasoids but are far more distressing psychologically. Hyperpigmentations such as melasma and lentigos are genuinely dreaded and are viewed as serious cosmetic defects which compromise social activities. Huge sums of money are spent on bleaching agents, some of which are toxic, while many others are only marginally effective.

Wrinkles, hated and feared in Western societies, are not only less frequent in Orientals but are less stigmatized as a sign of aging. Still, as the popula-

tion ages, wrinkles become coarser and more spoiling of appearance, especially in sunny areas. Thus, wrinkles are becoming a highly visible cosmetic defect, which are less likely to be viewed as a proud badge of age.

China is a huge country. In the South, climatic conditions are comparable to countries of Southeast Asia. In Northern China, where this study was carried out, meteorologic circumstances are quite different.

The weather is frequently dry and windy, predisposing to dryness.

Summers are hot and sunny, resulting in marked signs of photodamage in middle-aged adults, most of whom make no effort to protect themselves from the ravages of sunlight.

Changing social mores are also making people more conscious of their appearance as they become older.

It is against this background that we decided to evaluate topical tretinoin for the treatment of photoaged skin.

We attained results which compare favorably to those reported for other ethnic populations.

## MATERIALS AND METHODS

We recruited 27 volunteers, ages 35 to 67, of whom 23 were women.

All gave a history of excessive sun-exposure in childhood and in their teens. Working in the fields was a common background.

Each showed typical signs of moderate to severe heliodermatitis, namely, peri-orbital and perioral wrinkles, rough dry skin, dyspigmentations of various sorts and degrees, very spotty mottling, lentigos and blotches, loose, inelastic skin and uneven, coarse texture.

The subjects considered themselves handicapped cosmetically and were eager to participate in the study.

Treatment consisted of the nightly application of 0.05% tretinoin cream (Retin A<sup>®</sup>, Ortho Pharmaceuticals) for six to nine months, according to the specifications in the package insert and

comparable to usage in prior reports in other countries. Purpose Cream (Ortho Pharmaceuticals) was applied liberally in the mornings to combat dry, windy weather and to moderate the scaling and stinging often induced by tretinoin. The entire face was treated. Additionally, one hand and dorsal forearm was similarly treated once daily with 0.05% tretinoin cream.

The duration of treatment was six to nine months. One hand and forearm was treated with Purpose cream, as a non-medicated control.

Global evaluations of improvement were made monthly, along with assessments of adverse effects.

## RESULTS

### Adverse Events

Attention was specifically paid to the following changes; erythema, scaling, dryness, burning and itching. These were present to varying degrees in nearly all patients, generally making their appearance in the first few days, persisting over the next few weeks and slowly declining thereafter as the skin became accommodated. These reactions were more frequent and more intense on the face as compared to the hands and forearms.

Tightness was also a frequent complaint. Dryness and scaling tended to persist longer than other signs and symptoms, especially when the weather was windy.

After 4 to 8 weeks of trying to comply with the nightly tretinoin regimen, 8 of the 27 panelists decided to quit the study because of persistent side effects.

Burning and dryness were the most frequent and distressing complaints.

All the others completed the study, with minor difficulties exempt for occasional bouts of scaling for which we advised stopping treatment for a few days, using Purpose Cream generously in the drug-free periods.

### Clinical Evaluating of Improved Appearance

Beneficial effects were obtained more quickly and more markedly on the face as compared to the hands and forearms.

Fine wrinkles, especially around the eyes, were either completely effaced or appreciably diminished in the majority of subjects. Coarse deep wrinkles on the other hand, especially in older subjects, were mostly resistant to treatment, in the view of both the patients and the physician.

Fading and bleaching of dyspigmentations, along with a more uniform skin tone was perhaps the most successful aspect of this trial. Nearly every subject experienced a definite



Fig. 1a. Pretreatment photo showing fine lines, dyspigmentation, coarse surface and small bags under eyes.



Fig. 1b. After 24 weeks of treatments the surface is smooth, pigmentation has faded, texture is more uniform and bags under eyes are no longer evident.

lightening of hyperpigmentation, noticeable to friends and relatives as well as to the physician. However in several subjects who initially showed hyper-pigmented elevated seborrheic keratoses, no improvement occurred either in the degree of pigmentation or the lesion itself.

Another effect which most subjects found particularly pleasing, was replacement of a sallow, yellow complexion by a rosier color. This change in coloration was also apparent to the physician, though difficult to score.

In nearly every case, too, the texture and tone of the surface became smoother and softer to the touch. These are subjective assessments which the volunteers are better able to perceive than outside observers. While we did not have the subjects fill out detailed questionnaires for each cosmetic feature, they were asked to volunteer as much information as their experience allowed, whether positive or negative.

We concluded from listening and looking that the volunteers were particularly impressed by the manifest benefits in lightening hyperpigmentations, effacement of fine wrinkles, improved tone and coloration, and more uniform texture and smoothness.

### ***Hands and Forearms***

Except for some improvement of dryness and roughness, Purpose Cream by itself had no appreciable effect on any subject.

On the other hand, lightening of pigmented spots were, as on the face, was perceivable to be the most noticeable cosmetic benefit of Retin-A<sup>®</sup>. The rate of bleaching of dyspigmentations was slow and in a few cases non-apparent, even after 9 months. Overall the bleaching effect was real, but only modest.

Most experienced some improvement in surface smoothness and uniformity of skin tone. This too was noticeable but not dramatic.

Adverse side reactions were much less frequent and of lesser magnitude on the forearms as compared to the face.

So, while tretinoin was better tolerated on the hands and forearms, it was also less effective.

## **DISCUSSION**

Our results confirm that topical tretinoin can improve the appearance of photodamaged skin of Chinese persons.

Applied daily to the face for 6 to 9 months, we found substantial lightening of hyperpigmentations (mottling, blotches, lentigos), effacement of fine wrinkles, improved surface texture and smoothness and replacement of sallow skin with a rosier complexion.

On the hands and forearms, the cosmetic benefits were slower to develop and less impressive. The dry, windy meteorologic conditions in North China pose a challenge for the daily use of tretinoin, which by itself can provoke dryness, burning and erythema. These discomforts occurred in nearly all subjects. Eight of 27 panelists were unable to accommodate to these adverse events and dropped out of the study after one to two months.

In the rest, these signs and symptoms abated after a month or so, enabling completion of the study without undue difficulty.

As regards tolerance to potentially irritating substances, Japanese dermatologists have come to believe through clinical experience, that Oriental skin is more "sensitive" than that of Caucasoids. They emphasize that neurosensory purely subjective reactions such as itching, burning and stinging are more frequent and intense in Oriental skin. Though rigorous proof is not at hand, our drop-out rate is at least consistent with the notion that Oriental skin is more reactive to chemicals.

People in North China are not yet fully aware of the hazards of excessive exposure to sunlight and accordingly take no protective measures. Thus, heliodermatitis is very common in middle-aged adults and is destined to become much worse as the population ages. Although it is widely believed that melanin affords protection

against photodamage, most of our patients had a prematurely aged appearance with advanced signs of photodamage, namely, numerous deep wrinkles, laxity, multiple dyspigmentations and a sallow complexion. Whatever protection may be conferred by melanin, was certainly overwhelmed in our hot, dry windy climate with intensive solar radiation in summer.

Despite the difficulties in conducting this trial, we were able to show that topical tretinoin had the same beneficial effects in photoaged chinese skin that have been noted in many other studies in other cultures and climates.

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