

Mini Review

Evaluation of a New Cosmetic Combination for Melasma Treatment in Mexican Population

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Abstract

Background: Melasma is one of major concerns of the population, mainly among women, due to its hormonal background. In the Mexican population, with darker phototypes and the additional fact of indigenous ancestors in more than 90% of cases, melasma is more prevalent and difficult to treat. Many cosmetic products are being developed in order to improve the melasma condition; however, few of them have enough effectiveness and safety in dark phototypes.

Aim: Perform the evaluation of a new depigmenting regime for facial melasma treatment in Latin patients with Mexican origin.

Patients/Methods: Prospective, observational open study of 30 patients between 34 and 78 years (average 52,9 years) with long lasting melasma, of which 65% had received previous treatments. 27 patients completed the study and more than 90% were female patients.

Treatment regime was depigmentant serum (Neoretin Discrom® Control Serum, IFC SA) applied nightly and depigmentant cream with sunscreen (Neoretin Discrom® Control Gelcream SPF 50), in the morning. The evaluation methods included: Clinical images register (Standardized photographs were taken using RBX technology), dermatoscopic images register, brightness by chromameter (Minolta CR 400), MASI (Melasma Area Severity Index), review from two independent researchers, and the self-assessment from the patients.

Results: After the treatment a significant MASI score reduction was detected, the average MASI reduction was of 50% ($p < 0.0001$), and more than 65% of patients showed some degree of improvement in MASI score ($p < 0.0001$). Additionally, 77% of patients showed improvement of skin brightness and 90% of patients perceived an improvement in the self-assessment surveys. This regime had a very good tolerance and only a slight and transient erythema was observed in 23% of patients. We must also emphasize that the two independent researchers obtained statistically significant agreement ($p < 0.001$) after assessing clinical changes (improvement, worsening or absence of changes).

Conclusions: This new cosmetic regime has shown to be efficient and safety in the improvement of facial melasma, inducing lightening of hyper pigmentation in more than 65% of patients and very well tolerated in the Mexican population.

Therefore, after these observations we can recommend this depigmentant regimen for all skin types and mainly in darker skin types where other skin lightening products can worsen the melasma.

INTRODUCTION

Melasma is an acquired skin condition characterized by irregular brown or hyper pigmented patches located on the forehead, cheeks, chin and upper lip. The pathogenesis of melasma is not completely understood, but is thought to be influenced by genetics, UV exposure, thyroid dysfunction and hormonal influences from either pregnancy or hormonal therapeutic medications. Recent studies suggest that melasma is caused by subclinical inflammation [1,2] induced by ultraviolet (UV) radiation [2,3]. Skin inflammation, such as pronounced erythema, has been demonstrated objectively by colorimetry and thermography that can worsen the melasma pigmentation [2-5,6]. In addition, there is histological data demonstrating the presence of a moderate lymphohistiocytic infiltrate, increased mast cell infiltration in adjacent elastotic areas, augmented vascularity, and up regulation of pro-angiogenic factors [4,7].

Melasma is a distressing condition and has been shown

to impact a patients quality of life in several studies [1-3]. People of Latin descent comprise a vast array of skin colors and skin phototypes [1,2,8]. Similar, disorders of pigmentation, particularly melasma, occur more frequently in people of Latin origin when compared other populations specially in those populations with a great percentage of indigenous ancestors [1,2].

Melasma treatments must not be very aggressive in order to avoid skin irritation, because could worsen the melasma. Conventional treatment includes avoiding possible trigger factors, daily application of suitable photoprotection and topical bleaching products such as cosmeceutical or pharmaceutical products (like tretinoin and hydroquinone). In addition, other technologies such as lasers or Intense Pulsed Light (IPL) are also indicated for pigmentation disorders, usually in combination with bleaching products searching a synergic effect [9]. Linking to this topic, our protocol is appropriate for melasma with satisfactory results.

This regime (combining Neoretin® Gel cream SPF 50 and Neoretin® Discrom Control Serum) is proposed for skin whitening and improvement of skin texture. These products are based on RetinSphere® technology (Hidroxy-pinacolone retinoate and Retinol glycospheres) incorporating a whitening booster system (N-Acetyl Glucosamine, Niacinamide, Kojic acid). All these ingredients count on a wide scientific support as pigmentation regulators [10]. The formulation has a Moisturizing system, designed to reduce transepidermal water loss (TEWL) and due to its low molecular weight penetrates deeply; it captures and retains water on the skin's surface and releases it into the epidermis. In addition, it has ingredients with anti-irritant and anti-inflammatory properties. This regime reduces the stimulus and response of melanin synthesis.

Retinsphere® is the main technology of this new depigmentant regime and has a powerful lightening activity through several regulatory mechanisms of melanogenesis, acceleration of epidermal turnover and enhancement of penetration of other active ingredients. It has anti-inflammatory properties, as well as normalizes epidermal proliferation. In addition, it enhances the penetration of the other components of the cosmetic formulation [14]. This ingredient has demonstrated to increase skin elasticity and brightening, and to decrease wrinkles and pigmentation of photoaged skin [15]. Furthermore, other studies have demonstrated that Retinsphere® improves uneven pigmentation and telangiectasias [16].

This formula has demonstrated its efficacy, tolerability and safety in several previous studies. The successful preliminary results obtained in a pilot study [11] with 30 Caucasian and 10 Asian females were newly assessed in subsequent studies. In this preliminary study several parameters show a significant improvement, such as intensity of pigmentation (melanin index), brightness of skin (colorimetry) and the hydration of the skin (Corneometer®). Clinical improvement was observed in 70% Caucasian patients and 80% of Asian subjects. Other study in thirty Caucasian race subjects was published by Truchuelo et al., with excellent safety and effectiveness outcomes [12]. The patients were evaluated by split face, applying only vehicle with SPF on one side of the face and the active regime on the other side. They observed a significant reduction of MASI on the side treated with the new regime. The reduction of MASI at the end of the study on the side treated with the active treatment was 74% vs. a reduction of 55% on the side that received the vehicle with SPF, with this being a significant difference ($P = 0.009$). The authors highlight that the tolerance to the treatment with the new combination has been very satisfactory and they proposed that such regime could be compatible with sensitive skin.

There is another study in 80 Asian women with hyperpigmentation disorders, where the preliminary results with the same regime demonstrated significant improvement in skin brightness; lightening and anti-ageing effects compared to the control [13].

The main objective of this study was to evaluate the efficacy and tolerability of a cosmetic product with the combination of two retinoids in improving facial melasma in the Mexican population. The evaluation of clinical changes after using the product, as well as the degree of improvement perceived by investigator and

patient were deemed as secondary variables. Adverse events were monitored throughout the study.

STUDY POPULATION AND METHODS

In this prospective, open and observational study the patients acted as their own control before and after treatment. Thirty patients were recruited.

The inclusion criteria were: Women or men 18 years old or greater in good health at study entry, facial Melasma and Absence of treatment for melasma in the last 2 months.

The exclusion criteria were

Pregnant or on breastfeeding women and administration of another topical or systemic product that may interfere or affect the results.

TREATMENT REGIME

The treatment regime included a depigmenting serum and depigmenting cream plus sunscreen. Neoretin Discrom control Gelcream SPF50 was applied in the morning on a clean face, massaging until completely absorbed. In the evening, Neoretin Discrom control Serum was applied on a clean face with the same procedure.

CLINICAL ASSESSMENT

Standardized photographs were taken on each visit using Reveal System (RBX technology). We also recorded dermoscopic images (Dermlite II Pro) and we evaluated skin brightness with chromameter system (Minolta CR 400).

The Melasma Area and Severity Index (MASI) is the most commonly used outcome measure for melasma and it was developed to provide a more accurate quantification of the severity of melasma and changes during therapy. The MASI score is calculated by subjective assessment of 3 factors: area [1] of involvement, darkness, and homogeneity. The total score range is 0 to 48 [18].

Two independent researchers performed a photographs assessment. Subjective Global Investigator and Patient Global Assessment were performed at the end of the study.

STATISTICAL ANALYSIS

The comparison of the effects of the cosmetic product between pre and post-treatment were evaluated with semi quantitative or quantitative variables, depending on the parameters. For each variable in the study, a non-parametric Wilcoxon test (paired samples) was used to contrast the possible significant differences between after and before treatment, A p value less than 5% ($p < 0.05$) was considered as significant. All the calculations and tests were made by using a software SPSS, V21.0.

RESULTS

A total of 30 patients aged between 34 and 78 years old were included. 27 out of 30 completed the study. Average age was 52.9 years and more than 90% were female patients. Average follow up period was 3.11 months.

The improvement after treatment perceived by both



Figure 1 A significant clinical improvement of melasma was registered. The clinical images showed the skin condition improvement after treatment in some patients (Figure 1A,B). clinical improvement before and after three months

investigator and patient resulted in a very significant amelioration of melasma darkness ($p < 0.001$). More than 90% of patients observed some degree of improvement and more than 55% observed marked improvement (Figure 2). The two independent researchers obtained significant statistically agreement ($p < 0,001$) after assessing the photographs images changes (improvement, worsening, absence of changes).

Regarding the objective parameters evaluated

MASI score: After the treatment with the new depigmenting regimen, significant reduction of MASI score was detected in more than 65% of patients ($p < 0,0001$) (Figure 3). The average of the MASI scoring reduction was 50% ($p < 0.0001$).

Skin brightness: Significant increase ($p < 0.05$) of skin brightness detected by Chromameter was reached in 76,9% of patients (Figure 4) at the end of the treatment.

Dermoscopy findings: With dermoscopy we could evaluate superficial pigmentary changes and the vascular network under the pigment. Based on these observations, an improvement in pigmentation is registered in 57.7% of patients and the vascular network increases in 19.2% of them.

The combined treatment has been very well tolerated and no serious side effects were reported. A slight, transient erythema was observed in 23% of patients. Any patients drop out for side effects to the treatment (Figure 5).

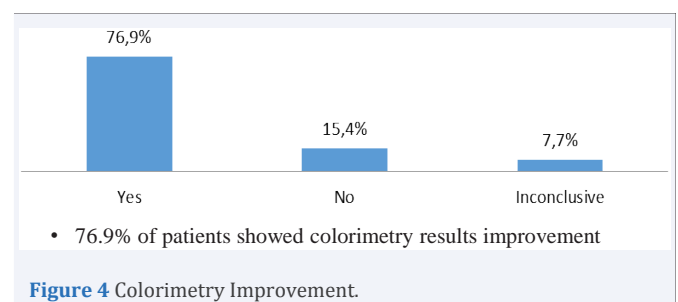
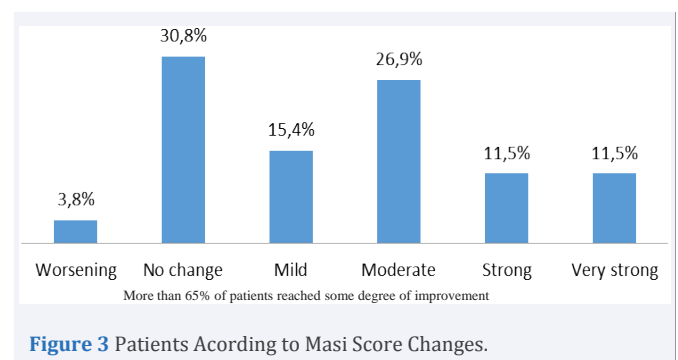
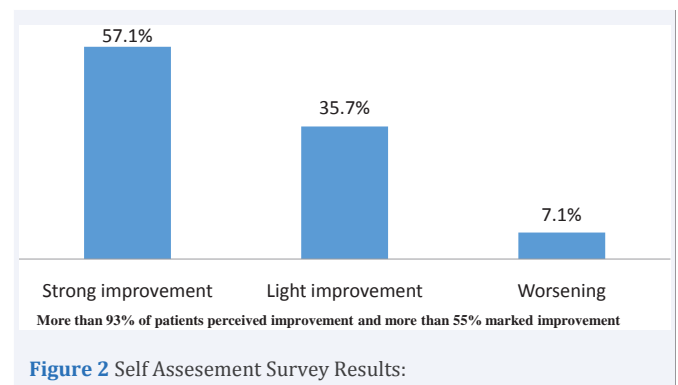
DISCUSSION

Melasma is a common disorder of hyper pigmentation that affects millions of people all over the world. Found most commonly in women with Fitzpatrick skin phototypes III to V [8] living in areas of intense ultraviolet (UV) light exposure, melasma is often difficult to treat and has a significant negative

impact on quality of life [1]. In Mexican population melasma is a very common skin disease, due to the skin phototypes and, more important, the indigenous origin. This fact not only causes melasma more frequently among Mexican population but also it is more difficult to treat, and furthermore, we can see worsening with conventional treatments, because of this reason.

The avoidance of exacerbating factors such as UV light and hormonal contraceptives and testing for underlying thyroid disorders can lead to improvement in certain subsets of patients. Recent studies, however, have shown that the underlying basis for melasma may be more complex than originally thought. These findings also provide new avenues for research into better understanding and treating this challenging condition [19].

Topical treatments are the most used for melasma, and we can find a large variety of products, both cosmetics and drugs for this purpose [20]. Tyrosinase is the rate-limiting enzyme in the process of melanin production, converting L-tyrosinase to L-3,4-dihydroxyphenylalanine (L-DOPA), and is the major target for many of the agents that have been developed for melasma. Many compounds exhibit multiple effects leading to decrease the hyper pigmentation.



Several topical retinoids have been used with some success in the therapy of melasma. The mechanism of action is thought to involve stimulation of keratinocyte turnover, inducing a decrease of melanosome transfer [20], and allowing greater penetration of other active ingredients. Tretinoin has been commonly used in the treatment of disorders of hyper pigmentation [19,20]. It is thought to inhibit tyrosinase transcription, interrupt melanin synthesis, inhibit tyrosinase-related proteins 1 and 2 (TRP-1 and TRP-2), and has been shown to decrease posttranscriptional levels of tyrosinase and TRP-1 after UVB exposure [20]. A randomized, vehicle-controlled study of 0.1% tretinoin versus vehicle cream applied nightly to the face of white women with melasma for 40 weeks reported that 68% of tretinoin-treated patients were rated as improved or great improved compared to just 5% of the patients treated with vehicle [22].

We advocate the use of retinoids due to its high effectiveness in patients with melasma without the problems related to the use of hydroquinone in dark phototypes [22,23]. However, retinoids could provoke skin irritation, causing itching, redness and flaking, and if they induce irritation, might worsen the melasma and reduce the patient's compliance. Retinsphere technology is based on retinoids which retain their therapeutic capacity with less or absent irritation than classic molecules.

In this observational study, the treatment with the new regime induced a very significant improvement in MASI and colorimetry measurement without significant adverse effects.

The use of this retinoids combination (hydroxypinacolone retinoate and retinol glycospheres) has demonstrated the improvement of hyper pigmentation in previous studies [11,12] and the tolerance was excellent, which is considered essential for any product to ensure a proper compliance.

In conclusion, this cosmetic regimen has demonstrated to be safe and effective for the treatment of melasma in Mexican population. It achieved a significant improvement of both subjective and objective parameters, and there were not significant side effects.

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