EFFICACY AND TOLERABILITY OF NEORETIN DISCROM CONTROL SERUM IN THE TREATMENT OF MELASMA

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SUMMARY

Objectives: To evaluate the efficacy and safety of Neoretin Discrom Control Serum for the treatment of melasma.

Methods: A clinical trial in 36 melasma patients treated with Neoretin Discrom Control Serum for 4 months. Patients were re-examined at weeks 4, 8, 12, 16; Facial pictures by digital camera were taken and were evaluated the improvement of melasma on the MASI scale, on dermoscopy, the change in Melanin index through the Mexameter, clinical side effects and patient satisfaction during and after treatment was noted.

Results: Melasma treatment with Neoretin Discrom Control Serum resulted in a 64% reduction in MASI (from 15.23 to 5.52) after 4 months of treatment. Melanin index measured by Mexameter also decreased after 4 months with a reduction rate of 30.4%. The most common undesirable effect is a stinging sensation (52.8%). Other side effects include itching, burning, redness, dry skin, scaling, acne, and hyperpigmentation. Side effects were encountered mainly in the first month and were mild-moderate. No serious side effects and no systemic side effects were detected. After 4 months of treatment, the patient's self-rated melasma lesions improved by 46%, with an average satisfaction score of 7.8/10**.**

Conclusion: Neoretin Discrom Control Serum proved to be an effective and safe product for the treatment of melasma. It should be combined with moisturizers and skin-soothing creams to minimize unwanted effects.

Keywords: *Melasma, MASI, retinoids.*

1. INTRODUCTION

Melasma is a common skin disorder characterized by gray-brown discolored patches of skin on areas of the face exposed to the sun. Melasma has complex pathogenesis, with many factors influencing its pathogenesis including genetics, sun exposure, hormone sensitivity, pregnancy, nutritional disorders, and in some cases related to drugs, cosmetics, etc.1 Melasma treatment is extremely difficult and recurrence is quite common. Currently, there are many melasma treatment methods including topical medications containing whitening agents, lasers, IPLs, biological peels, and oral medications,...2 In which, using topical agents containing lightening agents is the first choice for the treatment of melasma.

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Topical drugs include: hydroquinone, retinoids, azelaic acid, kojic acid, niacinamide,...3 Retinoids and their derivatives are effectively indicated. However, the use of topical retinoids often causes irritation, dry skin,… in patients. Neoretin Discrom Control Serum contains a formula of RetinSphere® (hydroxypinacolone retinoate and retinol glycospheres) combined with whitening agents N-Acetyl glucosamine, niacinamide and kojic acid. It has been proven to be well tolerated by several studies around the world. It reduces the local side effects of retinoids, increases the effectiveness in the treatment of melasma and some hyperpigmentation diseases compared to treatment with agents alone4.5. However, in Vietnam, this product has not been researched. Therefore, we conducted this study to evaluate the effectiveness and safety of Neoretin Discrom Control Serum for the treatment of melasma.

2. MATERIALS AND METHODS

2.1. Subjects

36 healthy male and female melasma patients aged over 18 years with no concomitant diseases at the National Hospital of Dermatology and Venereology from April 2021 to August 2021. Exclusion criterias included: Pregnant or nursing women, administration of topical or oral medications containing hydroquinone, tretinoin, steroids or oral medications containing Vitamin A agonists (isotretinoin, acitretin), sex hormones or administration of chemical peels, laser therapy within 3 months before the study.

2.2. Methods

Study design: A clinical trial study.

Materials: Neoretin Discrom Control Serum Booster Fluid 30 ml (Ingredients: Hydroxypinacolone retinoate 0.1%, retinol 1%, niacinamid 4%, N-Acetyl glucosamine 2%, kojic acid 4.8%, natriquest 0.5%, salicylic acid 0.15%, albatin 1%, alistin 0.5%, diffuporine 2%, hyromanil 3%, hydracare 5%, portulaca extract 3%), Endocare aquafoam gentle cleansing wash and Heliocare advanced gel SPF50, digital camera, Mexameter, Wood lamp, dermoscopy.

Treatment protocol:

The observation period was 4 months, organized into visits at baseline (T0), at one month (W4), at 2 months (W8), at 3 months (W12), and 4 months (W16).

Examination at T0 to determine the clinical melasma form, MASI scales, measure the melanin index by Mexameter. Full-face imaging under standard conditions and lesion assessment on dermoscopy.

Treatment: Patients washed their face daily with Endocare aquafoam gentle cleansing wash, used Heliocare advanced gel SPF50 sunscreen daily, applied Neoretin Discrom Serum Booster Fluid 30ml evenly over the entire face after washing the face in the evening.

Evaluation during and after treatment: Patients were re-examined at weeks 4, 8, 12, 16; Facial pictures by digital camera were taken and were evaluated the improvement of melasma on the MASI scale, on dermoscopy, the change in Melanin index through the Mexameter MX18 (Courage + Khazaka electronic), clinical side effects and patient satisfaction during and after treatment was noted.

Data analysis: Data were analyzed by SPSS 20.0. Descriptive data were described as numbers (percentage) and were used to test the differences by the chi-square test or Fisher's Exact test where appropriate.

3. RESULTS

3.1. Characteristics of the subjects

A total of 43 patients were recruited at the begining, 36 patients completed the study. 7 patients withdrew from the study due to SARS CoV2, acute urticaria or personal reasons. No patient withdrew from the study due to adverse effects experienced during treatment.

Table 1. Patient characteristics

Features		n	%
Gender	Female	35	97.2
	Male	1	2.8
Age (years old)	< 30	0	0
	30 - 40	9	25
	40 - 50	17	47.2
	≥ 50	10	2.8
	Average age: 45.3 ± 6.3		
	Age onset: 38.5 ± 6.5		
Average time of sun exposure per day (minutes)	< 15	3	8.3
	15 - 29	8	22.2
	30 - 60	9	25
	> 60	16	44.4
Other diseases	Endocrine disease	7	19.4
	Chronic disease	11	30.6
	Other pigmentary disorders	14	38.9
Family history of melasma	Yes	20	55.6
	No	16	44.4

Most of the patients participating in the study were female (97.2%), with a mean age of 45.3 ± 6.3 and a mean age of melasma onset of 38.5 ± 6.5. The age group of 40 - 50 accounted for the highest proportion (47.2%). Most patients had more than 60 minutes of sun exposure per day. Comorbidities included thyroid disease, ovarian cyst, hypertension, post-inflammatory hyperpigmentation ect. 55.65% of the patients had a family member with melasma.

Table 2. Distribution of study subjects according to clinical characteristics

Features		n	%
Clinical pattern	Malar	16	44.4
	Centrofacial	19	52.8
	Mandibular	1	2.8
Melasma type (according to wood's lamp assessment)	Epidermal	15	41.7
	Dermal	0	0
	Mixed	21	58.3

Most of the subjects had centrofacial melasma (52.8%) and malar pattern (44.4%). Based on wood's lamp assessment, mixed melasma was found in 21 patients (58.3%), followed by epidermal melasma in 15 patients (41.7%). None of the subjects was classified into the dermal melasma group.

3.2. Neoretin Discrom Control Serum's Melasma Treatment Efficacy

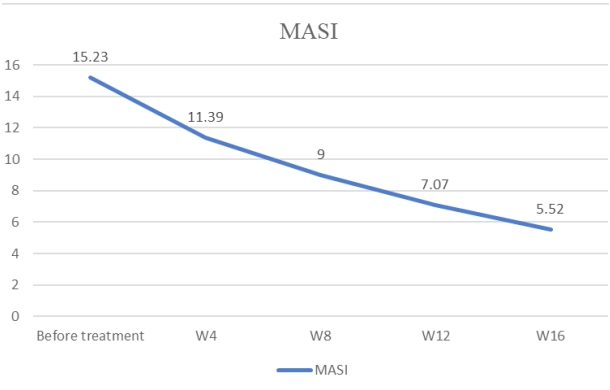
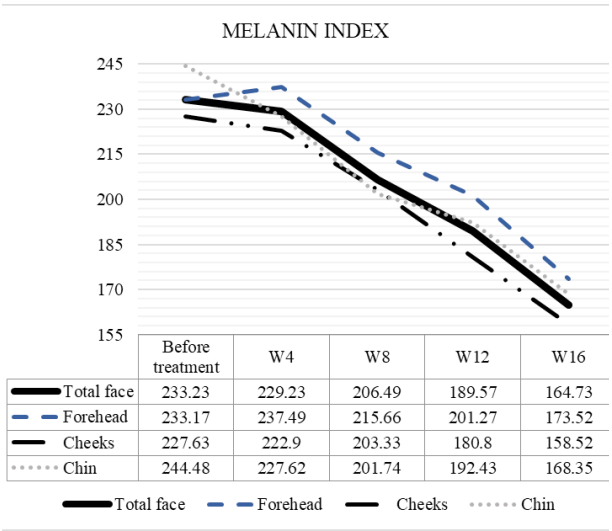


Chart 1. Improvement of MASI during treatment

The average MASI decreased significantly after 4 months from 15.23 to 5.52 (reduced by 63.8%). The difference in MASI over each month of treatment was statistically significant with $p < 0.001$. Many patients showed significantly clinical improvement after 4 months of treatment (Figure 1).

Figure 1. Patient L.T.H, 38 years old, evolution of melasma for > 10 years Photography before treatment (left) and after 4 months of treatment (right)



	Before treatment	W4	W8	W12	W16
Total face	233.23	229.23	206.49	189.57	164.73
Forehead	233.17	237.49	215.66	201.27	173.52
Cheeks	227.63	222.9	203.33	180.8	158.52
Chin	244.48	227.62	201.74	192.43	168.35

Chart 2. The improvement of melanin index in the whole face and each area through the Mexameter

Melanin index of the whole face and each area of the face (cheeks, forehead, chin) decreased after 4 months of treatment, the difference was statistically significant ($p < 0.001$).

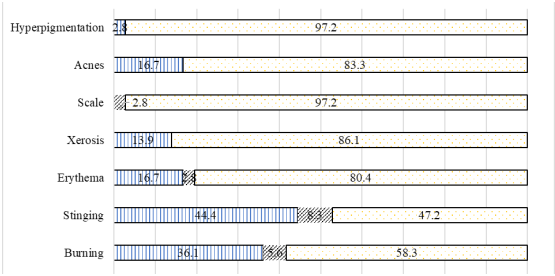


Chart 3. Patients' satisfaction

After 4 months of treatment, the average satisfaction level of the patients was 7.8/10, the lowest score was 4/10, the highest was 10/10.

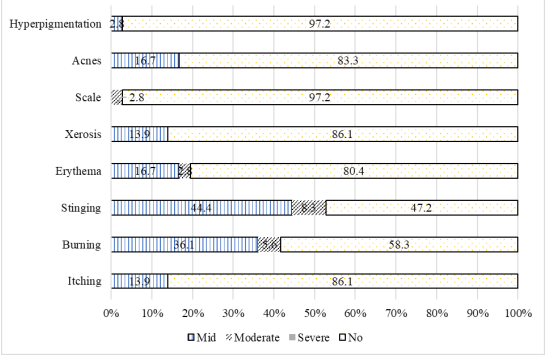


Chart 4. Improvement percentage according to the subjects' assessment

After 4 months of treatment, the average improvement of melasma according to the subjective assessment of patients was 46%. 1 patient self-assessed up to 75% lesion reduction. Melasma lesions of the patients improved at least 10%.

3.3. Tolerability of Neoretin Discrom Control Serum

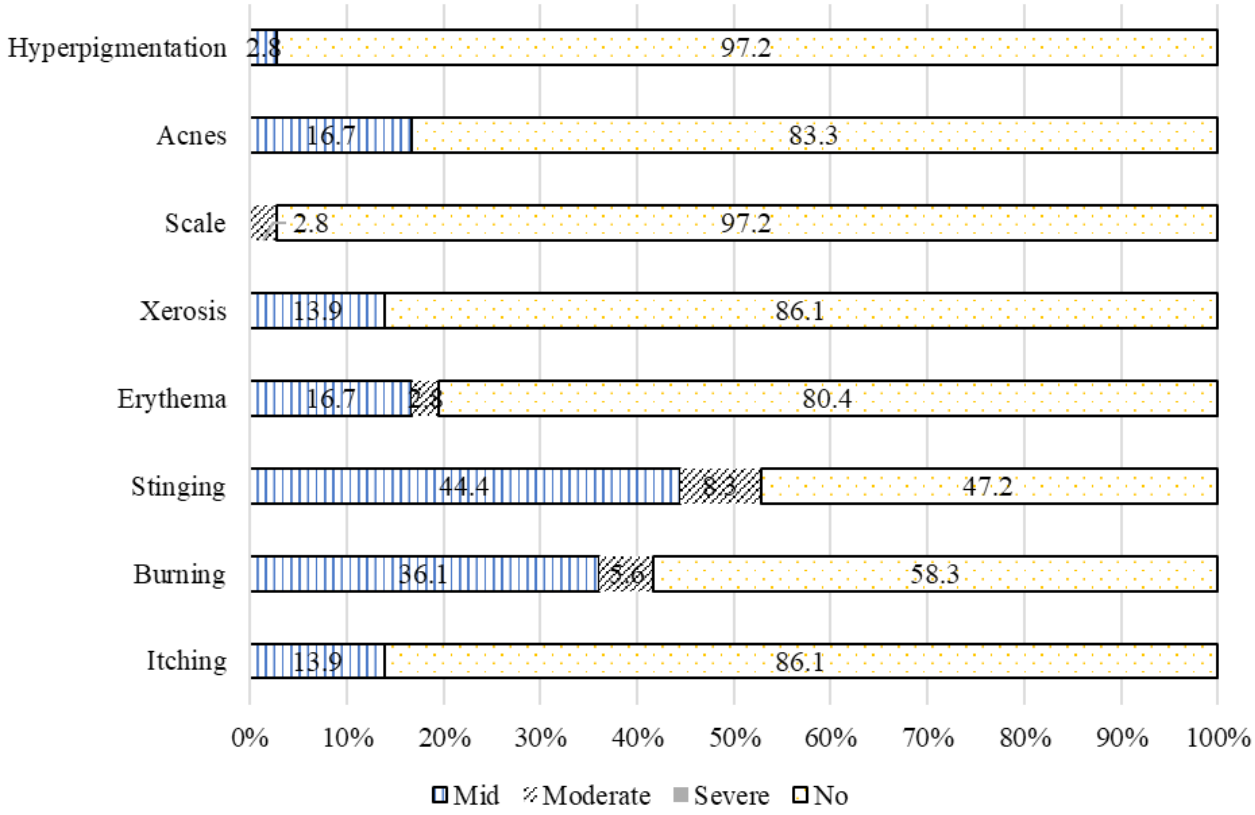


Chart 5. Prevalance of side effects

Stinging and burning sensations were the most common side effects (accounted for 52.8% and 41.7% respectively). Hyperpigmentation and scaling were the least common side effects, only seen in 1 patient (2.8%). Side effects were only mild to moderate.

4. DISCUSSION

Our clinical trial of 36 patients showed that Neoretin Discrom Control Serum significantly improved melasma lesions. The MASI decreased markedly over each month of treatment, with statistically significant difference. MASI is an index developed by Kimbrough Green et al. and is widely and specifically applied in the "guideline protocol for melasma clinical trials" to measure the degree of melasma, based on the percentage of relative surface of involvement (A), the intensity of darkness (D) of melasma, and the homogeneity (H) of the hyperpigmentation in 4 locations: forehead, 2 cheeks, and chin. In our study, 100% of patients achieved MASI improvement after 4 months of treatment. The mean MASI decreased from 15.23 to 9.00 after 2 months and to 5.52

after 4 months of treatment. Thus, after 2 months of treatment, MASI decreased by 40% and after 4 months of treatment, MASI decreased by 64%. This result is similar to the study of Cristina Garcia Millan et al (2018) using Neoretin Discrom Control Serum Booster Fluid 30ml in combination with Neoretin Discrom Control Gelcream SPF50 40g to treat 30 melasma patients in Mexico, after 3 months of treatment, the average MASI score decreased by 50%[4]. Another study by Maria Teresa Truchuelo also showed that the MASI reduction rate after 3 months of melasma treatment with Neoretin Discrom Control Serum was up to 74%.[5] The improvement in MASI in our study was greater than in other studies using retinoids alone in melasma treatment, with MASI improvement rates ranging from 32 to 47 %[6,7].

In this study, the average melanin index of the whole face and each area are measured by the Mexameter. Mexameter works based on the absorption/reflection of light on the skin, in which the melanin index is calculated by the intensity of light absorbed and reflected at 660 and 880 nm. The melanin index is an objective criterion used in monitoring and treating pigmentary diseases. The results of our study showed that the mean total melanin index of all patients over the months of treatment also decreased, the difference was statistically significant with $p < 0.05$, with the rate of decrease was 30.4% after 4 months of treatment. In which, the average melanin index of each area after 4 months of treatment also decreased significantly compared to the time before treatment ($p < 0.05$). This result supports and complements the change in MASI showing a good response of melasma treatment to the study product.

The undesirable effects, such as itching, burning, stinging, redness, dry skin, scaly skin, acne, hyperpigmentation were also evaluated. These were all local, mild-moderate side effects and occured within the first month of study. The most common side effect was a slight stinging sensation on the skin after using the product, in 19 patients (accounting for 52.8%). Burning was also a common symptom with a rate of 41.7%. Subsequent symptoms encountered with a lower rate included erythema (19.4%), acne (16.7%), dry skin, itching (13.9%). 1 patient-reported hyperpigmentation and one patient developed scaly skin after the first month of treatment (2.8%). These are the common side effects of using products containing retinoids. Side effects remedies include: temporarily discontinuing Neoretin Discrom Control Serum until skin recovers, reducing the frequency of application or quantity of serum per application, increasing extra moisturizer in case of xerosis. With the above simple actions, the side effects were quickly improved, no case was necessary to suspend treatment.

5. CONCLUSION

Neoretin Discrom Control Serum is an effective and safe product for the treatment of melasma, with significantly reducing MASI and melanin index after 4 months of treatment. The product is well tolerated with transient and non-serious local side effects that could be resolved by using moisturizers or skin-soothing cream.

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