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Non- Segmental Vitiligo Treatment using Narrow Band Ultraviolet B Alone versus Topical Psoralen- Narrow Band Ultraviolet B

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ABSTRACT

Background: With a frequency of 0.5–2% in the general population, vitiligo is a chronic acquired depigmentary condition that manifests as single or clusters of achromic macules and patches on various body parts.

Objective: This study aimed to **e**valuate the efficacy of topical psoralen-narrow band ultraviolet B (NB-UVB) treatment of non-segmental vitiligo patients in comparison with NB-UVB alone.

Patients and Methods: This prospective interventional study included forty non-segmental vitiligo (NSV) patients, divided into two equal groups. Group I received only NB-UVB sessions while group II treated with topical psoralen plus NB-UVB. Vitiligo extent tensity index (VETI) was used for disease severity evaluation. All patients received three sessions weekly for sixteen weeks. The participants were recruited from the Dermatology Outpatient Clinic of Vitiligo, Ain- Shams University Hospitals.

Results: Group I and II were statistically matching as regards age, sex, special habits, vitiligo family history, disease activity or duration and associated diseases. VETI scores showed highly statistically significant post-treatment improvement in both groups. However, no statistically significant difference could be detected in those receiving NBUVB alone versus psoralen plus NBUVB.

Conclusion: The combination of topical psoralen and narrow band UVB is a successful treatment option for non-segmental vitiligo that is well tolerated. Its effectiveness is comparable to narrow band UVB alone, but not better.

Keywords: NB-UVB, VETI, Topical psoralen and vitiligo.

INTRODUCTION

In vitiligo, a chronic, acquired, and progressive illness that affects 0.5–2% of the general population, achromic macules may show up alone or in groups on various body parts [1, 2]. It is asymptomatic but it can cause significant psychosocial distress in patients, ultimately affecting their self-esteem, inter-personal relationships, and even employment potentials [3].

The exact etiology of vitiligo has been attributed to many theories, the most prominent are autoimmune, oxidative, neural, genetic, viral and psychological theories [4].

According to the convergence theory, autoimmune melanocyte loss is caused by an interaction of environmental, genetic, and immunological variables [5].

Corticosteroids, immune-modulators, vitamin D3 analogues, various forms of phototherapy (UVB, PUVA and NB-UVB), excimer lasers, and surgery/transplantation are among the therapeutic methods utilised for vitiligo [6, 7]. However, the best course of action has not yet been determined [8].

The effects of NB-UVB on vitiligo were originally researched by **Westerhof and Nieuweboer-Krobotova** [9]. Although it is regarded the most efficient and risk-free first treatment for moderate and severe disorders, there have been reports of phototoxicity and probable carcinogenicity [10, 11]. An effect with two steps has been suggested. First, there is immunomodulation, which causes the immune response to melanocytes to be downregulated. The melanocytes are then propelled to go to the epidermis and begin producing melanin [12].

Fructus psoraleae, a popular herb used in traditional Chinese medicine, is the source of psoralen, a tiny molecule from the coumarin family of substances. The US Food and Drug Administration has given the PUVA therapy its blessing for use in clinical settings. Psoralen is a photosensitive substance that is used to treat vitiligo and psoriasis by exposure to sunlight or ultraviolet radiation. Tyrosinase activity and melanin production may be boosted by psoralen treatment in healthy melanocytes located close to the injured cells [13, 14]. This study aimed to evaluate the efficacy of topical psoralen- NB-UVB treatment of non-segmental vitiligo patients in comparison with NB-UVB alone.

PATIENTS AND METHODS

This prospective interventional study included40 NSV patients, recruited from Vitiligo Outpatient Clinic, Ain-Shams University Hospitals through the period from January 2018 to December 2018. We included patients whose ages ranged between 13 and 70 years, who did not receive any systemic vitiligo treatment for 2 months or, topical treatment for 1 month prior to study involvement.

Exclusion criteria: Individuals with photosensitive conditions such xeroderma pigmentosum, acute lupus erythematosus, and porphyria. Those exhibiting

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idiosyncratic reaction or history of sensitivity to psoralen compounds, as well as patients with present melanoma or any other invasive skin malignancies in the past or in the family history. Children under 12 years and those with extensive vitiligo or who showed history of resistance to any form of phototherapy.
Each participant underwent a comprehensive dermatological examination, including collecting their full personal past, present, and family history (FH).

Two equal groups, each included 20 patients:
Group I treated with NB-UVB alone, and **group II** treated with topical Psoralen plus NB-UVB in the form of topical 8-methoxypsoralen 0.03 g/15 ml (Ultra meladinin paint, Memphis Chemical Company, Cairo, Egypt) 30 minutes before photo session. All patients received 3 sessions weekly for 16 weeks. The UV-100L Waldman (Germany) lighting system that was being utilised has UVB lamps (TL01 lamp) with an initial dosage of 0.25 J/cm^2. Every two to three sessions, the dosage was raised by 10% to 20%, with a maximum dose of 5 J/cm^2. In both groups, one patch of vitiligo affected skin was treated by topical psoralen only without exposure to NB-UVB to evaluate its sole role.

Photos were taken, before and after the end of study, using digital EOS 1300D canon camera (Taiwan). Vitiligo activity was evaluated according to vitiligo disease activity (VIDA) score**,** at the start and end of the study. Lower VIDA scores indicate less activity **(15)**. Disease severity was assessed according to Vitiligo Extent Tensity Index (VETI). It generates a consistent and repeatable value by combining analysis of severity and extensity to quantify the amount of vitiligo **(16)**.

Ethical approval: The Ethics Committee of Faculty of Medicine, Ain Shams University granted the study approval. All participants signed an informed written consents after a thorough explanation of the goals of the study and submitted to detailed personal and past history questions including previous medications and periods of activity. The Helsinki' Declaration was followed throughout the study's conduct.

Statistical Analysis

The obtained information was looked through, coded, and put into SPSS version 23. When the distribution of quantitative data was parametric, the mean, standard deviations, and ranges were shown and when it wasn't, the median and interquartile range (IQR) were shown. Quantitative and percentage representations of qualitative characteristics were also used. Using qualitative data, the Chi-square test was used to compare groups. The Independent t-test was used to compare two independent groups with quantitative data and a parametric distribution, whereas the Mann-Whitney test was used for a non-parametric distribution. A non-parametric distribution and quantitative data were used to compare two matched groups using the Wilcoxon Rank test. The relationship between two numerical variables in the same population was measured by the Spearman correlation coefficient. A 95% confidence interval was used with a 5% allowable margin of error. P values $\leq$ 0.05 were regarded as significant.

RESULTS

This prospective interventional study included 40 patients; 18 males (45%) and 22 females (55%), their ages ranged from 13-65 years (mean 34.05 ± 13.25 years). As regards, disease activity using VIDA score, 32 patients were active (had new lesion in last 12 months) and 8 patients were stable (didn't had any new lesion in last 12 months), the duration of the disease ranged from 2-36 years. VETI score ranged from 0.12 - 5.52 (before treatment). As regards, vitiligo FH; 29 patients had negative and 11 had positive FH. Stress worsened the condition in 15 patients (37.5%) while had no effect on 25 (62.5%) patient. Thirty nine patients were smokers and one patient was non-smoker. Comparison between group I and II showed statistically non-significant differences as regards age ranges, sex, smoking and vitiligo FH, making both groups statistically matching. As regards disease worsening factor (stress), a statistically significant higher values of stress were recorded in group II in comparison with group I, while no other statistically significant differences were found as regards activity and duration of disease **(Table 1).**

Table (1): Comparison between group I and II as regards vitiligo worsening factor, activity and duration of disease:

		Group I treated with narrow band UVB only	**Group II treated with narrow band UVB + topical psoralen**	**Test value‡**	**p-value**	**Sig.**
		No. = 20	**No. = 20**			
Factor worsening disease (stress)	Absent	11 (55.0%)	4 (20.0%)	5.227	0.022	**S**
	Present	9 (45.0%)	16 (80.0%)			
Activity of disease (VIDA score)	Stable disease	4 (20.0%)	4 (20.0%)	0.000	1.000	NS
	Active disease	16 (80.0%)	16 (80.0%)			
Duration of disease (y)	Median(IQR)*	6.5 (4 - 15.5)	6.5 (3 - 10)	-1.222	0.222	NS
	Range	2 – 25	2 – 36			

Concerning VETI score between group I and II before and after treatment, there was statistically non-significant difference. Though, there was more improvement in group II than in group I after treatment, as indicated by higher change percent of VETI scores, however the fact that the difference was not statistically significant showed that none of the treatment methods was superior to the other **(Table 2).**

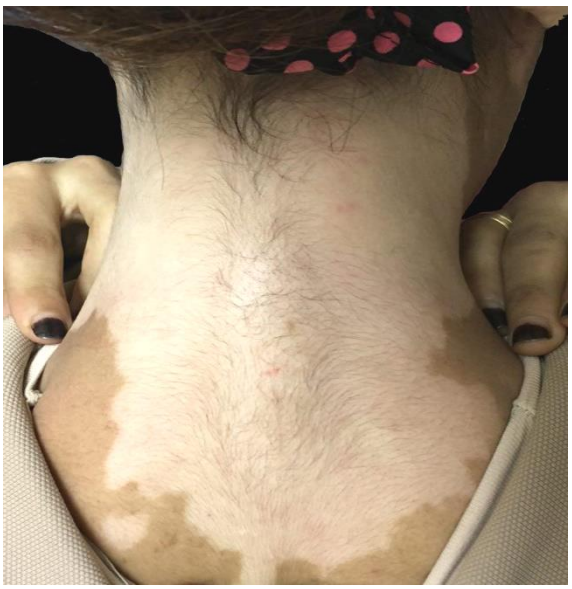
Table (2): Comparison between group I and II as regards VETI score before and after treatment:

		Group I treated with narrow band UVB only	**Group II treated with narrow band UVB + topical psoralen**	**Test value‡**	**p-value**	**Sig.**
		No. = 20	**No. = 20**			
VETI score before treatment	Median(IQR)*	0.610 (0.345 - 1.074)	0.601 (0.408 - 1.187)	-0.271	0.787	NS
	Range	0.119 – 5.519	0.228 – 3.350			
VETI score after treatment	Median(IQR)*	0.450 (0.265 – 0.838)	0.393 (0.26 - 0.742)	-0.135	0.892	NS
	Range	0.022 – 3.416	0.093 – 2.404			
Percent change of VETI score	Median(IQR)*	-23.295 (-40.64- -12.218)	-35.546(-41.242- -23.61)	-1.217	0.224	NS
	Range	-92.542 – 30.917	-73.729 – 23.246			

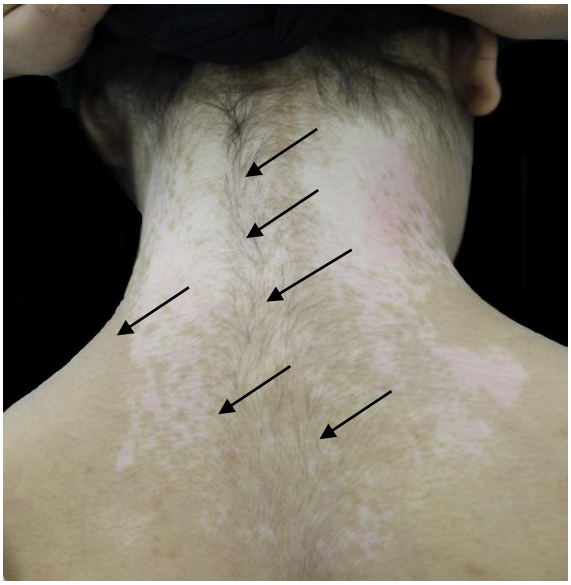
Comparison of base line and post-treatment values of VETI score, showed statistically highly significant improvement in both groups, indicating effectiveness of both treatment modalities NB-UVB as well as Psoralen– NB-UVB in vitiligo treatment (**Table 3 & Figures 1 & 2).**

Table (3): Comparison between VETI scores before and after treatment in each group:

		Before treatment	**After treatment**	**Test value‡**	**p-value**	**Sig.**
		No. = 20	**No. = 20**			
Group I Treated with narrow band UVB only	Median(IQR)*	0.610 (0.345 - 1.074)	0.450 (0.265 - 0.838)	**-2.875**	0.004	**HS**
	Range	0.119 – 5.519	0.022 – 3.416			
Group II Treated with narrow band UVB + topical psoralen	Median(IQR)*	0.601 (0.408 – 1.187)	0.393 (0.26 - 0.742)	**-3.845**	0.000	**HS**
	Range	0.228 – 3.350	0.093 – 2.404			

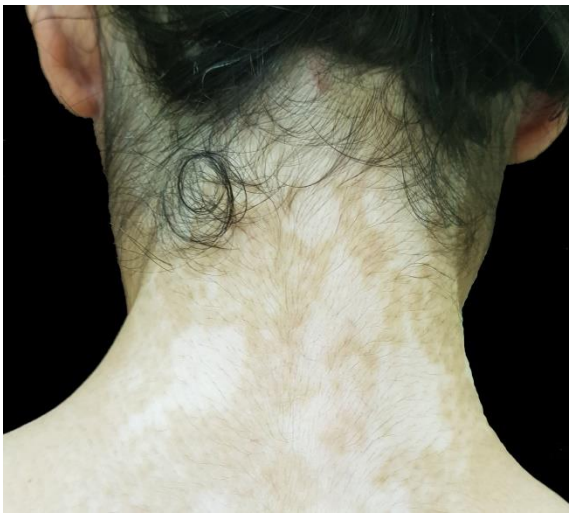


a. Before therapy

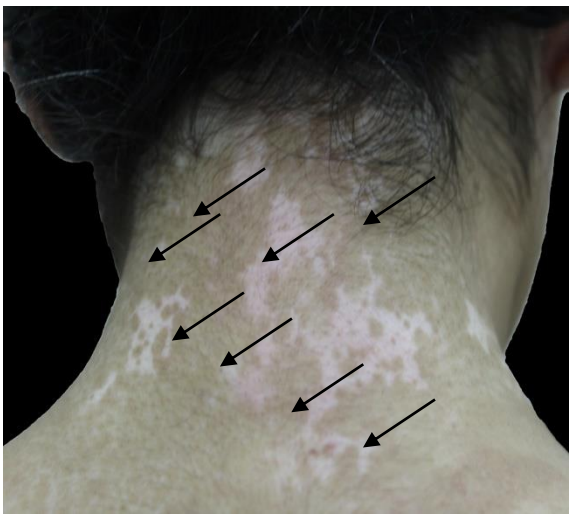


b. After therapy

Figure (1): Female-18-years-old with non-segmental vitiligo treated with narrow band UVB phototherapy on neck. (a) Before therapy. (b) After sessions, the arrows represents peri-follicular and marginal re-pigmentation.



a. Before therapy



b. After therapy

Figure (2): Female-19-years-old with non-segmental vitiligo treated with topical psoralen plus NB-UVB phototherapy on neck. (a) Before therapy. (b) After 48 sessions, the arrow represents peri-follicular and marginal re-pigmentation.

Baseline disease activity (VIDA score), showed statistically non-significant correlations with other studied parameters (sex, age, special habits, stress, vitiligo FH, VETI score before and after treatment and percent of change of VETI score) in all cases**.** Baseline and post-treatment VETI scores showed statistically non-significant relationships with all patients' variables [age, sex, special habits (smoking), disease worsening factors (stress), disease activity and FH or any other associated diseases]. Baseline and post-treatment VETI score of group I showed statistically non-significant correlations with all the studied variables. However, baseline and, post-treatment VETI scores in group II revealed a statistically significant relation with stress (P-value: 0.047 and 0.006 respectively), and statistically non-significant correlations with the other variables, previously mentioned.

Effect of topical psoralen alone on covered patch revealed that in 36 patients (90%) there was no response (re-pigmentation) and 4 patients (10%) had responded (slight re-pigmentation). Further investigation proved that those 4 patients to be in compliant, due to exposure to NB-UVB during sessions and were excluded from the study. Regarding the adverse effect in the two studied groups, few phototoxic reactions (erythema, vesicles and itching) during therapy, one patient from each group was followed, with no statistically significant difference between groups I and II. Sessions were temporarily stopped for those patients and soothing cream was used, then treatment was continued.

DISCUSSION

Vitiligo is a chronic acquired and progressive depigmentation disorder caused by melanin deficiency [(1)]. When compared to PUVA, narrow band UVB is both safe and effective. A breakthrough in NB-UVB phototherapy used a 311-313 nm light spectrum with a peak at 311 nm. It induces melanocyte differentiation and melanin production [(17, 18)]. Combination of psoralen and UV-A (PUVA) is a widely used treatment for NSV, although there are various issues that limit its application [(9)]. Thus another approach was tried by **El Mofty *et al.*** [(19)] and **Bansal *et al.*** [(20)] who used systemic psoralen with NB-UVB aiming to minimize the side effects and get better efficacy of NB-UVB**.**

This prospective interventional study included 40 patients who were divided into two equal groups: I and II, thirty two patients with active vitiligo (16 in each group) and 8 stable cases (4 in each group). All patients received three NB-UVB (311 nm) phototherapy sessions per week for 16 weeks. Group II applied topical 8-methoxypsoralen 30 minutes before photo session. All patients had one patch of vitiliginous skin lesion painted with topical psoralen only, without exposure to NB-UVB to evaluate its role.

Group I and II showed statistically non-significant differences, as regards age, sex, smoking habit, vitiligo FH, activity and duration of the disease and other associated disease, making both groups statistically matching and comparable. NB-UVB alone and topical psoralen plus NB-UVB therapy produced a statistically highly significant improvement in VETI score after treatment, 48 sessions, (P-value: 0.004 and 0.000 respectively). The improvement was in form of erythema, peri-follicular and/or peripheral re-pigmentation. However, comparison between group I and II as regards, change percentage of VETI score after treatment revealed statistically non-significant difference between both treatment modalities (P-value: 0.224), indicating equal effectiveness in vitiligo treatment. This could be due to improper sensitization of psoralen, as its peak to have a proper effect upon its use, occurs at 360 nm, which is not the condition with NB-UVB (311 nm). Our findings are consistent with earlier research on **El Mofty *et al.*** [(20)] who compared oral psoralen plus ultraviolet B (PUVB) versus UVB alone and resulted in equal clinical improvement with both modalities. However, they observed that PUVB required a lower cumulative dosage than UVB alone to produce the same response, the difference was not statistically significant, and PUVB considerably increased the incidence of phototoxic responses compared to UVB alone.

On the other side, our results do not support the previously published data of **Bansal *et al.*** [(19)]**,** who randomly allocated 45 vitiligo patients to receive either NB-UVB alone or oral psoralen P-NB-UVB treatment. NB-UVB was presented to both groups three times per week for a total of 60 sessions. By calculating the Vitiligo Area Severity Index (VASI) score, re-pigmentation was determined. In comparison with the NB-UVB group, the P-NB-UVB group had statistically substantially more re-pigmentation on the face and neck (P-value: 0.006) and hands (P-value: 0.007). The P-NBUVB group's percentage of VASI score reduction was statistically substantially higher (29.2% vs. 21.7%, P-value: 0.043). P-NB-UVB elicited a reaction earlier than NB-UVB by itself. Treatment response was also considerably better in the P-NB-UVB group (P-value: 0.005) once sunlight was eliminated as a confounding factor [(19)]. These different results could be explained with the longer treatment duration in this study (60 sessions versus 48 in ours), as well as the different application method of psoralen, oral in this study versus topical in ours.

Current study found a statistical significant correlation between baseline and post-treatment VETI scores, in group II, and the disease worsening factor (stress), while non-significant correlation was found between group I and the same variable. This may explain the statistically non-significant superiority of the change percentage of VETI scores in group II [-

35.546 (-41.242_ -23.61)], though it was higher than group I [-23.295 (-40.64- -12.218)], (P-value: 0.224).

CONCLUSION AND RECOMMENDATION

Topical psoralen combined with NB-UVB is a successful, well-tolerated treatment technique for NSV that showed statistically significant reduction in VETI score in a relatively short duration. However, its efficacy is equal to and not superior to NB-UVB alone. No major adverse effect was observed during the treatment with both methods, indicating the safety of topical psoralen plus NB-UVB. Topical psoralen alone without ultraviolet sensitization is ineffective when applied to vitiliginous skin. Further studies are recommended to assess the effect of long-term treatment of topical psoralen plus NB-UVB on a larger scale of patients.

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Competing interests: Nil.

REFERENCES

1. **Tarlé R, Nascimento L, Mira M *et al.* (2014):** Knowledge, beliefs, and perceptions of Turkish vitiligo patients regarding their condition**.** An Bras Dermatol., 89: 461-470.
2. **Krüger C, Schallreuter K (2012):** A review of the worldwide prevalence of vitiligo in children/adolescents and adults. Int J Dermatol., 51 (10): 1206-1212.
3. **Silverberg J, Silverberg N (2014):** Quality of life impairment in children and adolescents with vitiligo. Pediatr Dermatol., 31 (3): 309-318.
4. **Ezzedine K, Eleftheriadou V, Whitton M *et al.* (2015**): Vitiligo. Lancet,386 (9988): 74–84.
5. **Spritz R (2006):** The genetics of generalized vitiligo and associated autoimmune diseases. J Dermatol Science, 41: 3-10.
6. **Forschner T, Buchholtz S, Stockfleth E (2007):** Current state of vitiligo therapy--evidence-based analysis of the literature. J Dtsch Dermatol Ges., 5 (6): 467-475.
7. **Welsh O, Herz-Ruelas M, Gómez M *et al.* (2009):** Therapeutic evaluation of UVB-targeted phototherapy in vitiligo that affects less than 10% of the body surface area. Int J Dermatol., 48 (5): 529-534.
8. **Abd El-Samad Z, Shaaban D (2012):** Treatment of localized non-segmental vitiligo with intradermal 5-flurouracil injection combined with narrow-band ultraviolet B: A preliminary study. J Dermatolog Treat., 23 (6): 443-448.
9. **Westerhof W, Nieuweboer-Krobotova L (1997):** Treatment of vitiligo with UV-B radiation vs topical psoralen plus UV-A. Arch Dermatol., 133: 1525-1528.
10. **Njoo M, Bos J, Westerhof W (2000):** Treatment of generalized vitiligo in children with narrow-band (TL-01) UVB radiation therapy. J Am Acad Dermatol., 42: 245-253.
11. **El-Zawahry B, Bassiouny D, Sobhi R *et al.* (2012):** A comparative study on efficacy of UVA1 vs. narrow-band UVB phototherapy in the treatment of vitiligo. Photodermatol Photoimmunol Photomed., 28 (2): 84-90.
12. **Parsad D, Bhatnagar A, De D (2010):** Narrow band ultraviolet B for the treatment of vitiligo. Expert Rev Dermatol., 5: 445-449.
13. **Sapam R, Agrawal S, Dhali T (2012):** Systemic PUVA vs narrowband UVB in the reatment of vitiligo: a randomized controlled study. Int J Dermatol., 51 (9): 1107–1115.
14. **Ozkan I, Köse O, Ozmen I *et al.* (2012):** Effcacy and safety of non-laser, targeted UVB phototherapy alone and in combination with psoralen gel or calcipotriol ointment in the treatment of localized, chronic, plaquetype psoriasis. Int JDermatol., 51 (5): 609–613.
15. **Njoo M, Das P, Bos J *et al.* (1999):** Association of the Koebner phenomenon with disease activity and therapeutic responsiveness in vitiligo vulgaris. Arch Dermatol., 135 (4): 407-413.
16. **Feily A (2014):** Vitiligo Extent Tensity Index (VETI) score: a new definition, assessment and treatment evaluation criteria in vitiligo. Dermatol Pract Concept., 4 (4): 81-84.
17. **Rodrigues M, Ezzedine K, Hamzavi I *et al.* (2017):** Current and emerging treatments for vitiligo. J Am Acad Dermatol., 77 (1): 17-29.
18. **Kanwar A, Dogra S, Parsad D *et al.* (2007):** Narrow-band UVB for the treatment of vitiligo: an emerging effective and well-tolerated therapy. Int J Dermatol., 44: 57-60.
19. **Bansal S, Sahoo B, Garg V (2013):** Psoralen-narrowband UVB phototherapy for the treatment of vitiligo in comparison to narrowband UVB alone. Photodermatol Photoimmunol Photomed., 29 (6): 311-317.
20. **El Mofty M, Mostafa W, Esmat S *et al.* (2006):** Narrow band Ultraviolet B 311 nm in the treatment of vitiligo: two right–left comparison studies. Photodermatology, Photoimmunology & Photomedicine, 22 (1): 6-11.