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The efficacy of microphototherapy with a MedLight CupCUBE Grimed device in psoriatic patients with localized lesions

Neslihan YILDIRIM[1,*], Gül ERKİN[2]

[1]Turkey Community Hospitals Association, Mardin Midyat State Hospital, Dermatology Clinic, Mardin, Turkey
[2]Department of Dermatology and Venereology, Faculty of Medicine, Hacettepe University, Ankara, Turkey

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Background/aim: Psoriasis is a chronic skin disease. To reduce side effects associated with current treatment modalities, new treatment methods are required. Some clinicians have begun to use microphototherapy to treat psoriatic patients with a limited number of lesions (lesions affecting <10% of the body surface area).

Materials and methods: Microphototherapy is indicated in patients whose lesions persist despite systemic and topical treatment or when such treatment is contraindicated. Our study aimed to evaluate the efficacy of microphototherapy in psoriasis patients with localized lesions. Patients in this unblinded and prospective study were treated three times a week for 50 sessions using a MedLight CupCUBE Grimed microphototherapy device that emits an ultraviolet B (UVB) spectrum.

Results: Forty-five lesions in 23 psoriatic patients were treated. Treatment outcome was evaluated based on the Psoriasis Severity Index (PSI). PSI scores decreased significantly during the treatment.

Conclusion: The MedLight CupCUBE Grimed microphototherapy device was effective for the treatment of psoriasis patients with localized lesions. The device can administer UVB radiation to involved regions while protecting uninvolved regions and minimizing radiation dose. However, having to be administered by experienced technicians and the long time required for each treatment session are disadvantages of the technique.

Key words: Psoriasis, phototherapy, treatment

1. Introduction

Phototherapy is an important therapeutic modality commonly used for dermatological treatment. During the last two decades, there have been significant technological advancements in phototherapy. A new technique referred to as targeted phototherapy, concentrated phototherapy, focused phototherapy, or microphototherapy can be considered among the most important of such advancements. The disadvantages of conventional phototherapy devices include irradiation of unaffected areas and multiple frequent visits to clinics. It is also difficult to treat children and to treat such regions as genitalia and oral mucosa with these devices. Microphototherapy devices facilitate treatment of affected regions while protecting nonaffected regions. Additionally, these devices can reduce the number of treatment sessions and total duration of the treatment with increasing patient satisfaction. As opposed to conventional phototherapy, microphototherapy can be easily administered to genitalia, oral mucosa, and children (1). Several recent studies on the use of microphototherapy alone or in combination with topical drugs for the treatment of psoriatic patients have been published (2–9). The present study aimed to evaluate the efficacy of targeted UVB phototherapy using a MedLight CupCUBE Grimed microphototherapy device in the treatment of psoriasis patients with localized, plaque-type lesions.

2. Materials and methods

2.1. Patients

Patients who were admitted to the university hospital clinic of dermatology were evaluated for the study. Patients aged ≥10 years with chronic, plaque-type psoriasis and lesions affecting ≤10% of the body surface area were included in this prospective and unblinded study. Patients were included in the study providing that they did not receive systemic therapy such as methotrexate, cyclosporine,

* Correspondence: drnesli23@hotmail.com

biological agents, or any topical agent during the previous month or oral retinoid treatment during the previous 6 months. Exclusion criteria were pregnancy, lactation, and the presence of photosensitive disorders such as porphyria and xeroderma pigmentosum. Based on these criteria, 27 patients with chronic, plaque-type psoriasis were included in the study; however, 4 of the patients discontinued the therapy.

2.2. Phototherapy device

Microphototherapy was administered using a MedLight CupCUBE Grimed device, which uses nonexcimer technology to deliver UV radiation (Figures 1a and 1b). The light source was a 150-W high-pressure spherical burner that emits both UVA and UVB radiation. To benefit from the device's UVA emission, a filter must be placed on the device. However, only UVB radiation was administered during the study. The spectral irradiance of the device is shown in Figure 2. The light is concentrated within the UVB wavelengths of 300–350 nm, with a peak at 311 nm. The radiation field of the system varies from 10 mm to 40 mm. The UVB dose administered by the device is 30 mJ/cm^2 at a distance of 1 cm.

2.3. Treatment protocol

All lesions were irradiated with narrowband UVB (NB-UVB) phototherapy 1 cm away from the lesion. For lesions >1 cm in diameter, the area was treated with multiple applications side by side in accordance with the lesion diameter. Regardless of skin phototype and lesion diameter, the initial duration of treatment was 10 s and the initial treatment dose was 300 mJ/cm^2. The duration of treatment was increased 2 s and the dose was increased 60 mJ/cm^2 in every session. The therapy was applied three times a week

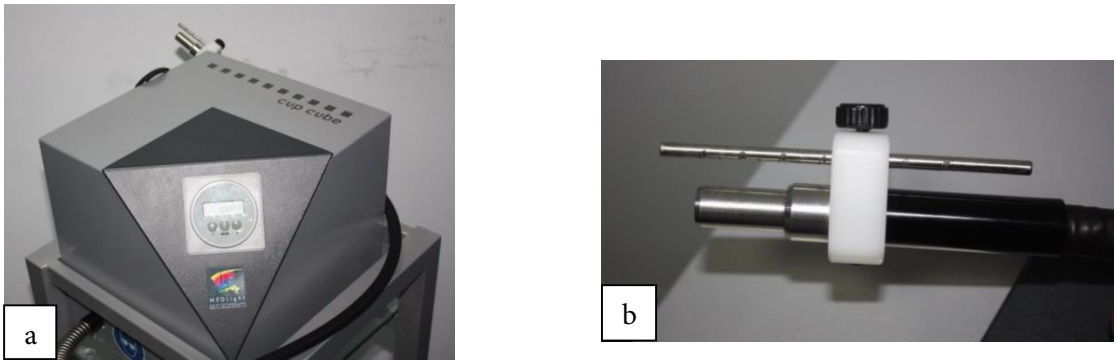

Figure 1. The MedLight CupCUBE Grimed microphototherapy device (a) and its light-transmission cable and distance adjustment bar (b).

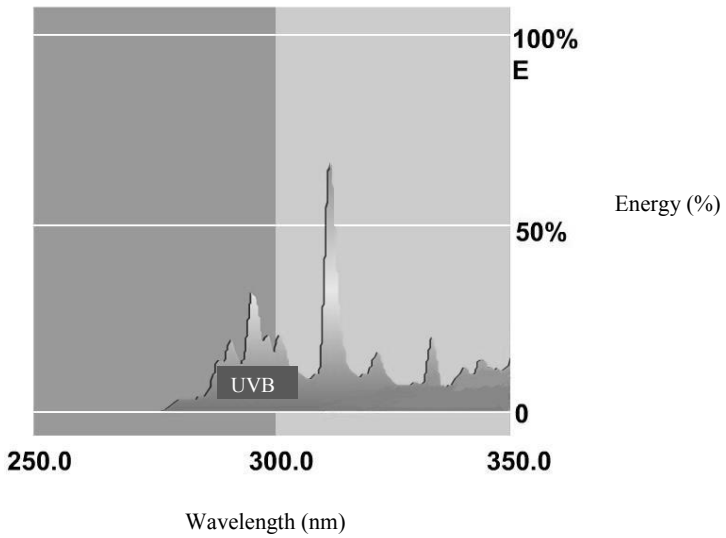

Figure 2. The UVB spectrum of the MedLight CupCUBE Grimed microphototherapy device.

on nonconsecutive days for 50 sessions in each patient. The treatments were administered by a phototherapy technician. To reduce the severity of scales of the plaques, the patients were advised to apply solid petrolatum to the lesions on nontreatment days and to wash the treatment areas before UV irradiation. Just before each UV treatment session, liquid petrolatum was applied to increase UV transmission. The duration of each subsequent treatment session was increased until mild/moderate erythema was observed. When severe erythema or bulla was observed, the treatment was not administered. During the subsequent treatment session if erythema or bulla regressed, the treatment was administered at the previous dose, but if no regression was observed, the treatment was administered for 2 s less than the previous session.

2.4. Assessment

The Psoriasis Severity Index (PSI) was used to evaluate treatment outcome. PSI is a modified Psoriasis Area and Severity Index (PASI) score used to assess erythema, induration, and desquamation on a scale of 0–4 (0: none; 1: mild; 2: moderate; 3: severe; 4: very severe). The maximum possible total PSI score is 12. As opposed to PASI, PSI ignores calculation of area; therefore, each lesion is assessed individually and the PSI score only provides information about a single lesion (5). However, both patient- and lesion-based scores were evaluated in this trial. If the patient had 2 or more lesions and these were being treated, their PSI score was accepted as the mean sum of the values for each lesion that was calculated before treatment, at session 36, and at session 50. At the end of session 50, PSI 50% (50% reduction in PSI score) was accepted as the required minimum response. If complete improvement was observed before session 50, the treatment was terminated early, whereas therapy was prolonged or switched to another treatment modality if after session 50 the response to treatment was inadequate. Treated plaques did not receive any topical or systemic therapy during the study. During the course of treatment, the largest diameter of each lesion was measured using a ruler and standardized photographs were obtained using a CanonEOS D450 digital camera at baseline and at treatment sessions 12, 24, 36, and 50.

2.5. Statistical analysis and ethics committee and Ministry of Health approval

SPSS v.21.0 for Windows (SPSS, Inc., Chicago, IL, USA) was used for all statistical analyses. At the end of the study, the primary endpoint was reduction in the PSI score. When parametric assumptions were not provided, lesion diameters and PSI scores were analyzed using Freidman's test. If there was a significant difference, then Wilcoxon's test was used for pairwise comparison. Wilcoxon test results were interpreted according to the Bonferroni-corrected P value. Differences in numeric variables between independent groups were analyzed by using the Mann–Whitney U test when parametric assumptions were not provided. The chi-square test was used to determine whether there were differences in categorical variables between independent groups. Relationships between the quantitative variables were calculated using Pearson's correlation coefficient. The level of statistical significance was set at $P < 0.05$.

This study received permission from Hacettepe University Faculty of Medicine Local Ethics Committee Clinical and Pharmaceutical Research on 22.11.2012 (Issue number: 06-03). The present study also received approval from the Ministry of Health with tracking number 806637 on 24.01.2013.

3. Results

The study included 23 patients of whom 13 (56.5%) were female and 10 (43.5%) were male. The mean age of the patients was 33.17 ± 13.22 years (10–62). Of all, 6 patients had an additional systemic disease including asthma (n = 1), epilepsy (n = 1), inactive hepatitis B carrier (n = 1), nonalcoholic steatohepatitis (n = 1), hypothyroidism (n = 1), and rheumatoid arthritis (n = 1). Among the patients, 8 patients had a family history of psoriasis in first- or second-degree relatives. None of the patients had psoriatic arthritis.

Totally, 45 lesions in the 23 patients were treated, 21 (46.7%) of which were localized on the elbow region, 17 (37.8%) on the knee, 3 on the abdominal region, and 1 each on the thigh, leg, buttocks, and sacrum region respectively. Localization of the lesions is shown in Figure 3. Eighteen patients had multiple psoriatic lesions. In 11 of 18 patients, the value of PSI scores in each lesion changed in different proportions during the treatment sessions. However, the changes in these scores did not seem to differ significantly. As for the remaining 7 patients, despite more than one lesion on the same patient, the lesions responded in the same way to the treatment (Table 1).

The mean lesion diameter and PSI score at baseline and at 4 time points during the course of treatment are shown in Table 2. In terms of lesion diameter, there was no improvement until session 36. In other words, there was no significant improvement in lesion diameter between sessions 0 and 12, 12 and 24, 24 and 36, 0 and 50, 0 and 36, or 24 and 50; however, a significant decrease in lesion diameter was observed between sessions 36 and 50 ($P < 0.05$).

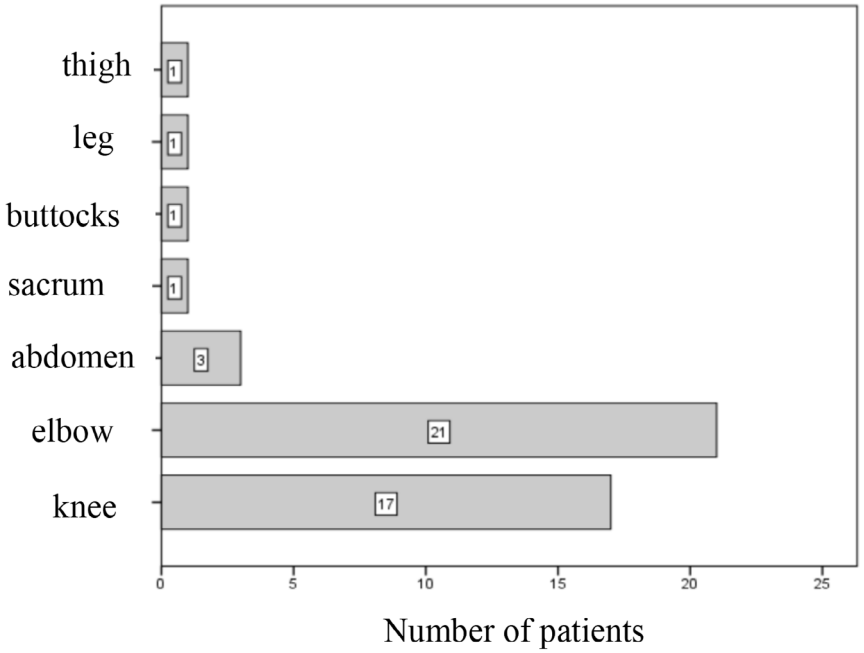

Figure 3. Localization of the 45 psoriatic lesions.

At the end of treatment session 50, the mean PSI score for the 45 lesions decreased from 5.6 to 3.07 (Table 2) and this difference was significant ($P < 0.05$). PSI scores at baseline and at sessions 36 and 50 are shown in Figure 4. The rate of PSI improvement for the 45 lesions was 31.71% at session 36, followed by 45.7% at session 50 (Table 3). Similarly, the rate of PSI decrease for the 23 patients was 45.8% at session 50 (Table 3). At the end of treatment sessions, 4 of the 23 patients exhibited complete clearance (PSI 100%, the percentage of decrease in the PSI score is 100, Table 4). In contrast, in 3 patients the PSI score never changed during the treatment sessions (PSI 0%, the percentage of decrease in the PSI score is 0). The remaining 16 patients responded to the treatment in varying degrees, but they did not reach the target PSI, 50%. However, they were very close to the target with mean PSI change of 46.6% at the end of session 50. All in all, 14 (60.9%) of the 23 patients achieved PSI ≥ 50% (Table 4).

The only observed side effect of the microphototherapy treatment was blister formation at session 45 and it was seen only in 1 of the 23 patients (Figure 5).

4. Discussion

To the best of our knowledge, the literature does not include any studies on the use of the MedLight CupCUBE Grimed microphototherapy system for the treatment of psoriasis or any other dermatological disease. It is known that UVB suppresses the proinflammatory cytokine pathway by decreasing interleukin (IL) 12, interferon-gamma (IFN-γ) and IL-8 expression, and can selectively reduce proinflammatory cytokine production by T cells (10). In contrast, since IL-4–producing T cells are resistant to the cytotoxic actions of UVB, IL-4 levels increase in psoriatic skin following UVB irradiation (11). Decreased IFN-γ expression and increased in IL-4 production after UVB irradiation lead to decreased local immunoreactivity, which forms the therapeutic effects of UVB on psoriasis. Moreover, UVB irradiation has inhibitory effects on the IL-23/IL-17 axis, which exhibits an important pathway in psoriasis pathogenesis (12). In conclusion, UVB therapy is associated with downregulation of type 1 and type 2 IFN signaling pathways (IL-12, IFN-γ, IL-8) and suppression of the IL-23/IL-17 axis while immunosuppressive cytokines as IL-4, IL-6, IL-10 increase.

Several studies have examined UV microphototherapy for psoriasis, but the findings are inconsistent (2–9). Asawanonda et al. (2) administered irradiation with targeted UVB phototherapy (Dualight) in 13 patients three times a week and reported clearance of localized psoriatic lesions after 4 weeks of treatment. Lapidoth et al. (3) achieved improvement using the BClear UV device and UVB irradiation administered twice a week to 28 patients for 6–18 sessions (mean number of sessions: 10). They reported a decrease in PSI scores of 73% after 6 weeks and 63% after 16 weeks, and they concluded that UVB microphototherapy was effective for the treatment of psoriasis. Toll et al. (7) treated 15 patients with chronic plaque psoriasis using the BClear Targeted PhotoClearing System twice a week for a maximum of 13 sessions. The mean Scaling Erythema Induration (SEI) score decreased

Table 1. PSI scores for the 45 psoriatic lesions in 23 patients.

Number of patient	Lesion number	Lesion	PSI 0	PSI 36	PSI 50
N1	2	L1	7	4	4
		L2	7	5	4
N2	2	L1	4	0	0
		L2	3	0	0
N3	1	L1	6	3	3
N4	3	L1	3	2	2
		L2	3	3	2
		L3	3	2	2
N5	1	L1	9	9	7
N6	2	L1	7	1	0
		L2	6	2	2
N7	2	L1	3	3	3
		L2	3	3	3
N8	2	L1	5	5	5
		L2	5	5	5
N9	1	L1	7	0	0
N10	2	L1	6	5	3
		L2	6	5	4
N11	4	L1	8	6	4
		L2	8	6	4
		L3	8	5	5
		L4	8	5	3
N12	2	L1	6	6	3
		L2	6	6	3
N13	1	L1	7	6	5
N14	2	L1	4	0	0
		L2	3	0	0
N15	2	L1	4	4	3
		L2	6	4	4
N16	2	L1	8	5	4
		L2	7	5	4
N17	3	L1	6	3	5
		L2	6	5	4
		L3	6	4	4
N18	2	L1	3	0	0
		L2	4	1	1
N19	2	L1	4	6	0
		L2	8	6	0
N20	1	L1	5	5	5
N21	2	L1	6	6	6
		L2	6	7	6
N22	2	L1	6	5	5
		L2	6	5	5
N23	2	L1	4	4	3
		L2	6	4	3

Table 2. Mean diameter and mean PSI scores for the 45 psoriatic lesions.

Number of sessions	Diameter (cm) (mean ± SD)	PSI (mean ± SD)
0	3.85 ± 1.59	5.60 ± 1.72
12	4.00 ± 1.57	
24	3.95 ± 1.92	
36	3.94 ± 2.31	3.89 ± 2.18
50	3.31 ± 2.39	3.07 ± 1.94

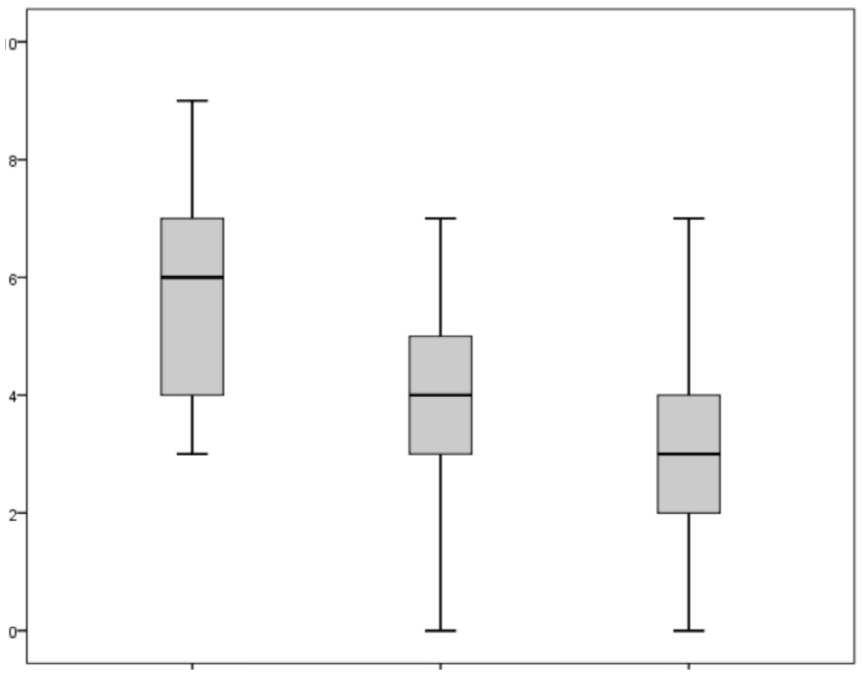

Figure 4. PSI scores at baseline, session 36, and session 50.

Table 3. The percentage of decrease in the mean PSI score for the 45 psoriatic lesions and in the 23 patients.

Range of sessions	PSI decrease (%) in 45 lesions (mean ± SD)	PSI decrease (%) in 23 patients (mean ± SD)
0–36	31.71 ± 36.21	33.05 ± 35.78
36–50	18.50 ± 31.24	15.00 ± 23.74
0–50	45.65 ± 33.12	45.75 ± 34.17

from 5.7 to 3.0 after a month of treatment. They concluded that UVB microphototherapy is an efficient and safe method for treating persistent plaques in psoriatic patients while sparing healthy skin regions. In 2011, Nishida published the results of targeted NB-UVB phototherapy using a flat-type lamp in 6 psoriasis patients with resistant plaques. They applied therapy with an initial dose of 70% of the minimal erythema dose, with a 20% increase at each subsequent session once or twice a week. At the end of the study, they reported that all lesions of the tested patients were responsive to NB-UVB phototherapy using the flat-type lamp (8).

Table 4. The mean PSI decrease according to the patients.

23 patients	The mean PSI decrease
3 of 23 patients	0%
4 of 23 patients	100%
6 of 23 patients	<50%
10 of 23 patients	≥50%

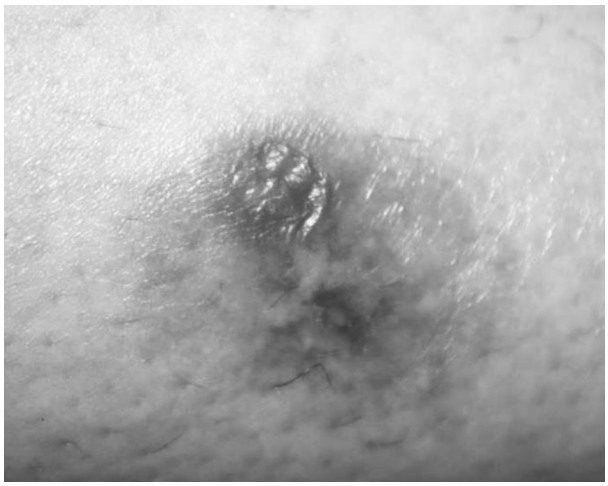

Figure 5. Blister formation in a psoriasis patient.

To increase the efficacy of microphototherapy, it can be combined with other therapies. Ozkan et al. (6) investigated the efficacy of adding topical therapies to microphototherapy in 30 patients with psoriasis. The patients were randomly divided into 3 groups: microphototherapy alone, psoralen gel plus microphototherapy, and calcipotriol plus microphototherapy. The researchers reported that the addition of calcipotriol ointment to microphototherapy enhanced the therapeutic effects of phototherapy in the treatment of patients with plaque-type psoriasis. In another trial, Amornpinyokeit et al. included 10 stable psoriasis patients who were randomized to receive either targeted NB-UVB alone or 8-methoxypsoralen (8-MOP)/NB-UVB to two separate areas within the same lesion. The improvement in disease activity as reflected by PSI score during the treatment was significantly better in the combination group. The mean remission time of lesions that were cleared by 8-MOP/NB-UVB was 8 weeks, while it was 4.67 weeks in lesions that were cleared by NB-UVB alone. Thus they concluded that addition of 0.1% 8-MOP cream to targeted NB-UVB significantly enhances the therapeutic effects of the light treatment without increasing the incidence of adverse effects (9).

Excimer lasers, excimer nonlasers, and monochromatic excimer nonlaser light (MEL) sources are the other microphototherapy methods. There are several studies on these devices. In a study with a large group of patients, Feldman provided data on 51 subjects who obtained at least 75% improvement in the lesions with 308-nm excimer laser treatment. They reported that 308-nm excimer laser treatments appear to offer relapse-free periods for psoriasis patients with localized lesions that are comparable or better than those offered by standard topical therapy regimens (13). MEL sources can be used to treat mild to moderate psoriasis, palmoplantar psoriasis, and palmoplantar pustular psoriasis (14,15).

Treatment with microphototherapy can cause various tolerable adverse effects including erythema, blistering, hyperpigmentation, erosion, burning, and itching (3,6,16–18). Therefore, in the present study the patients were asked about the occurrence of any of these side effects. According to the patients, the radiation was generally well tolerated. The only observed side effect was blistering in 1 patient and thus dose escalation was performed until session 50 in 22 patients. Dose escalation was used in order to ensure that as many of the patients as possible would benefit from the treatment. As a result, 60.9% of the patients had an improvement (the percentage of decrease in the PSI score is ≥50%). Moreover, 4 of the 23 patients had complete clearance (the percentage of decrease in the PSI score is 100%) at the end of treatment.

The study has some limitations. Firstly, the minimal erythema dose was not calculated. A standard therapy dose

and a standard duration of treatment were administered to all patients. Therefore, beginning the treatment with a low UVB dose might increase the number of sessions. Having a small number of patient groups and lacking a control group are the other limitations. Due to the fact that the treatment was time consuming and laborious and it required coming to the hospital three times a week, 4 patients who initially participated to the treatment apart from our study group of 23 patients discontinued the treatment.

In conclusion, the present findings show that targeted UVB radiation administered using a MedLight CupCUBE Grimed microphototherapy device at an emission range of 300–350 nm and a peak of 311 nm was effective for the treatment of psoriatic plaques. Furthermore, the findings indicate that targeted UVB phototherapy is an effective treatment option in psoriasis patients who do not benefit from topical therapy and who have limited numbers of lesions. In particular, microphototherapy eliminates exposing unnecessarily large areas of the body to radiation; however, this therapy must be administered by experienced technicians/clinicians. Thus, microphototherapy is more expensive and time-consuming than other treatment methods, especially in patients with lesion diameter >1 cm who require multiple treatment sessions. In addition, microphototherapy requires patients to come to the hospital at least twice a week. As a result of these challenges, we recommend the addition of topical therapies (topical corticosteroid, topical calcipotriol, topical retinoid, topical immunomodulator) to microphototherapy as a way to decrease the number of in-hospital sessions. We think microphototherapy is especially appropriate for patients with psoriasis who do not benefit from topical therapy, for those who develop side effects due to such treatment, for those of whom topical therapy is contraindicated, and for those with lesions that cannot be easily reached.

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