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SHORT REPORT

Fully home-based methyl aminolevulinate daylight photodynamic therapy for actinic keratosis of the face or scalp: A real life open study

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Abstract

Methyl aminolevulinate daylight photodynamic therapy (MAL DL-PDT) is highly efficacious for the treatment of nonhyperkeratotic actinic keratosis (AK), even when partially performed at home. To evaluate the long-term effectiveness, safety, and patient-reported outcomes of MAL DL-PDT performed completely by the patient in real life conditions. An open prospective study was conducted in Spain among patients diagnosed with at least five AK lesions on the face or the scalp. Patients received instruction and information in infographic format to perform MAL DL-PDT at home. All had been treated with 30% urea daily for 7 days before the day of MAL DL-PDT. Meteorological conditions on the day of the treatment and adverse effects were recorded. Patients underwent follow-up, and a second session of home-based MAL DL-PDT if deemed necessary, 3, 6, and 12 months after the initial treatment session. The study population consisted of 22 patients (19 men and three women, mean [standard deviation, SD] age, 72.05 [6.96] years). A complete response was observed in 47.7% of AK lesions at 3 months ($p < 0.001$) and 65.9% ($n = 199$) at 12 months ($p < 0.001$). Olsen grade II lesions showed the highest rate of response (76.07% at 12 months). The mean (SD) actinic keratosis area and severity index score decreased significantly from 4.99 (2.43) at baseline to 2.33 (1.01) at 12 months ($p = 0.0234$). Adverse effects were mild and expected. A majority of patients were "satisfied" or "very satisfied" with the treatment instruction provided (90.9%) and the treatment outcome (72.7%). MAL DL-PDT can be applied at home like any other topical treatment for AK. Our results indicate good long-term effectiveness, a high level of patient satisfaction, and no significant side effects.

KEYWORDS
actinic keratosis, daylight, photodynamic therapy

1 | INTRODUCTION

Actinic keratosis (AK) is the most frequent diagnosis at outpatient dermatology clinics in Spain,[1] and warrants particular attention given its potential to develop into squamous cell carcinoma.[2]

Current treatment options for AK include surgical excision, cryotherapy, photodynamic therapy (PDT), and topical application of fluorouracil, imiquimod, diclofenac, or tirbanibulin.[3] Daylight PDT (DL-PDT) is not among topical therapies for AK because it is performed in dermatology clinics, where the affected area is prepared by curettage, photosensitizer is applied by dermatologists or nurses, and the area is subsequently irradiated.[4]

To determine whether PDT could be applied by the patient themselves, we assessed the utility of a home-based methylaminolevulinate (MAL) DL-PDT protocol similar to that previously tested in Germany,[5] but performed completely by the patient, without prior in-patient curettage of the treatment area with an abrasive pad.

2 | PATIENTS AND METHODS

A prospective, observational open study was performed at the Dermatology Service of the Miguel Servet University Hospital in Zaragoza and Barbastro Hospital in Huesca, Spain, between September 2019 and December 2021. Adults aged ≥18 years who were diagnosed with at least five Olsen grade I and II AK lesions on the face or scalp and were candidates for DL-PDT treatment were eligible to participate.

The study was approved by the Clinical Research Ethics Committee of Aragon (EPA18/029).

Patients were instructed to perform DL-PDT at home by applying 30% urea cream to the AK area for 7 days prior to DL-PDT. Subsequently, on a sunny day they applied MAL cream (160 mg/g Metvix®) to the treatment area, waited 30 min before going outside for 2 h between 11 a.m. and 5 p.m., and then finally washed the treated area and protected it from the light. Patients were provided with oral and written (infographics) instructions on the treatment protocol.

Clinical data were collected and a cutaneous clinical exam was performed, during which the number, location, and Olsen grade for each AK lesion, as well as the actinic keratosis area and severity index (AKASI) and Actinic Keratosis Quality of Life Questionnaire (AKQoL) score, were recorded.[6] Patients completed a questionnaire indicating the date and the time at which each of the different steps of the protocol were performed, as well as patient-reported outcomes.

Efficacy was evaluated by counting the number of persistent and new AK lesions and their corresponding grade by comparing photographs taken at baseline and at each follow-up visit (3, 6, and 12 months after the DL-PDT session). Data on adverse effects and additional treatments required during follow-up visits for preexisting or new AK lesions were also collected.

All data were analyzed using SAS software (version 9.3 for Windows).

3 | RESULTS

The study population consisted of 22 patients: 19 (90.5%) men and 3 (9.5%) women. The mean (standard deviation, SD) age was 72.05 (6.96) years. Half of the patients were phototype II and the other half phototype III. Three patients (13.6%) were receiving immunosuppressive therapy with azathioprine during the course of the study. Nine patients had a history of nonmelanoma skin cancer (45.0%).

The mean (SD) number of AK lesions per patient at the beginning of the study was 12.50 (4.34). AK lesions were located on the face in eight cases (36.4%), on the scalp in eight cases (36.4%), and on the face and scalp in six cases (27.3%). Assessment of Olsen grade revealed 130 (47.3%), 117 (42.5%), and 28 (10.2%) grade I, II, and III lesions, respectively. Seven patients (31.8%) had not undergone prior treatment, whereas 15 patients (68.2%) had received at least one, including cryotherapy (36.4%), diclofenac (27.3%), 5% imiquimod (9.1%), 3.75% imiquimod (13.6%), DLPDT (4.5%), and surgery (4.5%).

Weather on the day of treatment was sunny in 17 cases (81%) and partially cloudy in four cases (19%). The mean (SD) outdoor temperature was 19.89°C (7.75).

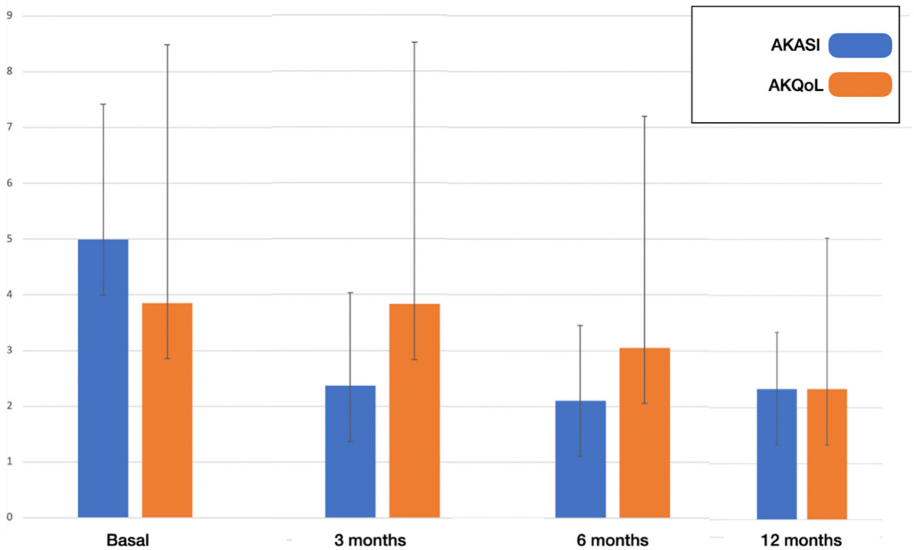
The mean (SD) number of persisting, resolved, and new AK lesions was 6.41 (4.74), 6.09 (4.44), and 0.27 (0.63) after 3 months of follow-up. After 6 months of follow-up, 4.64 (3.32) lesions persisted and 0.27 (0.77) new lesions were observed. After 12 months of follow-up, the mean (SD) number of persisting, resolved, and new AK lesions was 4.00 (2.76), 9.05 (3.76), and 0.73 (1.86), respectively.

A complete response was observed in 199 AK lesions (65.9%) 12 months after baseline (Table 1). A significant decrease in the Olsen grade of the AK lesions was also observed, as shown in Table 1.

TABLE 1 Home-based MAL DL-PDT: global reduction in the number of AK lesions according to Olsen grade, and number of lesions for which a complete response was observed

No. of AK lesions (% reduction from baseline)	Visit 1 (Basal)	Visit 2 (3 months)	Visit 3 (6 months)	Visit 4 (9 months)
Grade I	130	75 (42.31%)	63 (51.53%)	61 (53.08%)
Grade II	117	50 (57.26%)	26 (77.78%)	28 (76.07%)
Grade III	28	22 (21.43%)	19 (32.14%)	14 (50%)
Complete lesion response		134 (47.7%)	178 (62.2%)	199 (65.9%)

Note: For all Olsen grades significant reductions ($p < 0.001$) in the number of AK lesions were observed for all follow-up visits compared with baseline, and for visits 3 and 4 with respect to visit 2 ($p = 0.0359$ and $p = 0.0032$, respectively).



	AKASI	AKQoL
BASAL	4.99 (SD:2.43)	3.85 (SD:4.63)
3 Months	2.37 (SD:1.66)	3.83 (SD:4.68)
6 Months	2.1 (SD:1.35)	3.05 (SD:4.15)
12 Months	2.33 (SD:1.01)	2.33 (SD:2.69)

FIGURE 1 Evolution of the AKASI and AKQoL scores at the different visits, baseline, 3, 6, and 12 months.

Mean AKASI score was significantly lower at all follow-up visits compared with baseline ($p < 0.001$). However, no significant differences in mean AKQoL score were observed between visits (Figure 1).

Nineteen (86.36%) patients required a second session of home-based methyl aminolevulinate daylight photodynamic therapy (MAL DL-PDT): 8 (36.36%) at 3 months; 7 (31.82%) at 6 months; and 4 (18.18%) at 12 months.

Patients rated the mean (SD) pain level during treatment at 0.90 (2.32) on a numeric rating scale of 0–10. Local treatment-associated adverse events included erythema in 16 cases (72.7%), mild peeling and swelling in 7 (31.8%), crust formation (grades I and II) in 5 (22.7%), and vesicles/pustules (grade I) and erosion/ulceration (grade I) in 1 (5.3%).

Twenty patients (90.9%) were satisfied or very satisfied with the treatment instructions received and 16 patients (72.7%) were satisfied or very satisfied with the overall outcome after 3 months of follow-up.

4 | DISCUSSION

The present study demonstrates a response rate of 65.9% 12 months after a DL-PDT protocol performed completely by the patient (1 or 2 sessions), together with a decrease in mean AKASI score from 4.99 to 2.33 ($p = 0.0234$).

We observed a significant decrease in Olsen grade for all AK lesions, with the greatest decrease observed for grade II lesions. Patients reported no significant side effects and good satisfaction with the treatment.

DL-PDT offers a simpler alternative to conventional PDT, as the light exposure stage is managed by the patient themselves, without medical supervision.[4] In an open label study conducted in Germany by Karrer et al.,[5] patients rated home-based MAL DL-PDT as satisfactory or very satisfactory, specifically valuing the treatment effectiveness (88%), skin appearance posttreatment (80%), and the instructions received to carry out the treatment at home (98%). After 3 months of follow-up, 62% of overall lesions were completely clear. Patient-reported adverse effects were both mild and expected. We obtained similar findings in the present study. In the study by Karreret et al.,[5] scaling and hyperkeratosis were removed by the investigator at the baseline visit by curettage or using an abrasive pad. This was not performed in our study to ensure that the entire procedure could be carried out by the patient themselves, like any other topical AK treatment. Moreover, previous studies have reported no differences in effectiveness or tolerability in patients that undergo curettage or chemical keratolytic pretreatment with 40% urea cream before PDT.[7]

A systematic review of patient-reported outcomes following topical treatment of AK found that treatment adherence, patient satisfaction, and improvement in overall quality of life were better with simpler and shorter duration treatment regimens.[8] DL-PTD can be easily self-administered without professional assistance: treatment is completed within a single day and can be repeated at 3, 6, or 12 months of follow-up as deemed necessary, depending on the disease course.[9]

In conclusion, self-administered DL-PDT is an effective and safe technique that can be useful in patients who require this treatment periodically. Individualizing each case can help decentralize care from the hospital setting and simultaneously empower patients.

AUTHOR CONTRIBUTIONS

All persons designated as authors had participated in the work to take public responsability in its contents. Miguel Fernando García-Gil, Tamara Gracia-Cazaña, Laura Bernal-Masferrer, Paulina Cerro-Muñoz, and Yolanda Gilaberte contributed to the preparation of manuscript and critically modified. Miguel Fernando García-Gil and Tamara Gracia-Cazaña contributed in the preparation of figures. All authors contributed to the article and approved the submitted version.

CONFLICTS OF INTEREST

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

INFORMED CONSENT

Written informed consent has been obtained from the patient.

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