

Daylight photodynamic therapy for Bowen's disease^{☆,☆☆}



Dear Editor,

Bowen's disease (BD) is considered an indolent neoplasm with high cure rates after non-surgical treatments, which are often the first-line therapy.¹

The effectiveness of daylight photodynamic therapy (dPDT) in skin tumors has been demonstrated in studies with basal cell carcinomas.² Moreover, two case reports of BD treatment with dPDT showed complete response in three BD lesions.^{3,4} To date, no prospective studies have attempted to assess dPDT efficacy in BD treatment. The aim of this clinical trial was to assess the efficacy of dPDT for BD lesions at three months of follow-up.

A prospective study was conducted with consecutively selected samples among patients with histological diagnosis of BD. The treatment was performed between May 2016 and May 2017, in all seasons of the year.

The session followed the photographic registration protocol prior to treatment, with a camera (Canon® Powershot SX 500 IS) and a digital dermoscope (Fotofinder®). A sunscreen with organic filter (SPF 30) was applied on sun-exposed skin areas. Fifteen minutes later, the lesion surface was prepared by gentle removal of scales and scabs by curettage. A thin layer of 16% MAL cream was applied to the lesion. Patients started the daylight exposure within 30 min of the photosensitizer precursor application, and the exposure continued for two hours in an area within the hospital grounds.

Patients received one cycle of dPDT consisting of two treatment sessions, one week apart. The weather conditions, temperature, and maximum daily ultraviolet index (UVI) for Porto Alegre (Brazil) were obtained from the website of the Center for Weather Forecasting and Climate Studies.⁵

Treatment efficacy was assessed three months after dPDT. The primary endpoint was complete response, determined by clinical evaluation. Lesion responses were classified as complete, partial response (< 25%, 25–75%, or >75% response), or no response. The clinical assessment, conducted by a dermatologist, considered the presence of persistent erythema, hyperkeratotic areas, reduction of lesion size, and other dermoscopic data such as the occurrence of typical dotted or glomerular vessels.

The pain score was recorded each 30 min during the daylight exposure period and weekly following the treatment, by telephone questionnaire. It was scored using a visual analog scale ranging from 0 to 10 (0=no pain, 10=worst pain ever felt). In the evaluations, the main signs and symptoms were queried.

Nineteen patients, with 24 BD lesions, were included in the study (Table 1). Ten lesions were located on the lower

Table 1 Demographic characteristics of patients.

	Total (n = 19)
Age, mean (± SD)	69.7 years (± 10.6 years)
Gender, n (%)	
Male	12 (63.2%)
Female	7 (36.8%)
Transplanted, n (%)	
Yes	6 (31.6%)
No	13 (68.4%)
Comorbidities, n (%)	
Yes	15 (79.0%)
No	4 (21.0%)
Phototype, n (%)	
II	16 (84.2%)
III	2 (10.5%)
IV	1 (5.3%)

limbs, five on the head/neck area, five on the trunk, and four on the upper limbs. The majority of the lesions received the dPDT sessions between 10 a.m. and 2 p.m. ($n=16$; 66.7%), on sunny or partially cloudy days ($n=15$; 62.5%). The mean temperature was 19.91 °C (± 5.2) at the first session and 17.54 °C (± 4.6) at the second session. The mean ultraviolet index (UVI) was 3.25 (± 2.8).

Three months after dPDT, six lesions (25%) showed a complete clinical response, eight (33%) lesions showed > 75% partial response, four (8%) presented 25–75% partial response, two (8%) showed < 25% partial response, and four (8%) presented no response.

Lesions that presented a better response were located on the sun-exposed area, like the upper limbs and head/neck area ($p=0.01$); however, no specific group of patients benefiting from the technique was observed (Table 2).

The pain score perception during treatment was 0 in 79.2% of the treated lesions ($n=19$), with a median visual pain score of 0 (range 0–3) in both sessions. The adverse effects most frequently reported by the patients were scaling and redness.

The findings of this study suggest that dPDT is a feasible alternative treatment for BD in selected cases. Complete response was found in six lesions after three months of follow-up, demonstrating that some cases would benefit from dPDT. Moreover, in 14 (58.3%) lesions improvement was observed in more than 75% of the lesion area, supporting its use as a neoadjuvant alternative. However, these findings for dPDT show that, when compared to cPDT, there were fewer complete response cases, demonstrating that the latter might still be generally preferable for BD patients.¹

Sample size and lack of a control group were limitations of the study, as well as the follow-up time. Future studies evaluating efficacy in a longer follow-up may corroborate the findings of this study. It is also assumed that re-treatment of lesions that have partially improved may increase the proportion of lesions with complete response over a long-term follow-up.

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^{☆☆} Study conducted at the Hospital de Clínicas de Porto Alegre, Porto Alegre, RS, Brazil.

Table 2 Comparison between good responders (clinical response > 75% or complete) and less responsive lesions with regard to clinical and climatic data after three months of follow-up.

	Response ^a		p-Value*
	<75%	≥75%	
	(n = 10)	(n = 14)	
Sex, n (%)			0.73
Female	5 (45.5)	6 (54.5)	
Male	5 (38.5)	8 (61.5)	
Age, years, mean (± SD)	70.6 (± 2.8)	67.1 (± 2.7)	0.39
Lesion size, mm, mean (± SD)	19.7 (± 8.1)	21.0 (± 15.8)	0.87
Transplant recipient, n (%)			0.89
Yes	4 (40.0)	6 (60.0)	
No	6 (42.9)	8 (57.1)	
Comorbidities, n (%)			0.93
Yes	8 (42.1)	1 (57.9)	
No	2 (40.0)	3 (60.0)	
Climatic condition, n (%)			0.83
Sunny and/or partially cloudy on both applications	6 (40.0)	9 (60.0)	
Other combined conditions involving cloudy or rainy days	4 (44.4)	5 (55.6)	
UVI, mean (± SD)	2.8 (± 2.8)	3.6 (± 2.8)	0.43
Skin type, n (%)			0.24
II	9 (42.9)	12 (57.1)	
III	0.00	2 (100.0)	
IV	1 (100.0)	0.00	
Body site, n (%)			0.01
Head/neck	1 (20.0)	4 (80.0)	
Trunk	5 (100.0)	0	
Lower limbs	4 (40.0)	6 (60.0)	
Upper limbs	0	4 (100.0)	

^a Chi-squared test for sex, transplant recipients, climatic condition, phototype, and body location variables; Student's *t*-test for age and lesion size variables; Mann-Whitney *U*-test for UVI variable.

* $p \leq 0.05$.

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Authors' contributions

Carla Corrêa Martins: Statistical analysis; conception and planning of the study; drafting and editing of the manuscript; collection, analysis, and interpretation of data; participation in design of the study; intellectual participation in the propaedeutic and/or therapeutic conduct of the studied cases; critical review of the literature; critical review of the manuscript.

Renato Marchiori Bakos: Approval of the final version of the manuscript; conception and planning of the study; drafting and editing of the manuscript; collection, analysis, and interpretation of data; participation in design of the study; intellectual participation in the propaedeutic and/or therapeutic conduct of the studied cases; critical review of the manuscript.

Manuela Martins Costa: Conception and planning of the study; drafting and editing of the manuscript; participation in design of the study.

Conflicts of interest

None declared.

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Melanoma risk factors in a Latin American population

Dear Editor,

Malignant melanoma (MM) is a skin tumor associated with a high mortality worldwide. The five-year survival rate is 95% if melanoma is detected early and only 5% for metastatic melanoma.¹ In Colombia, the national registry reported an increased incidence of melanoma from four to six cases per 100,000 people in merely four years.² This highlights the importance of identifying melanoma risk factors, especially in Latin-American countries where the distribution of histopathological subtypes of melanoma is divergent with the reports in other countries, where acral lentiginous melanoma (ALM) is the most frequent MM subtype.³ Although a possible association with trauma has been reported, this association has not been clearly demonstrated.^{4,5}

Considering the aforementioned, a case-control study was performed between 2010 and 2014 in the population seen at the Federico Lleras Acosta Dermatology Center, a dermatological referral hospital in Bogotá, Colombia. Data from patients histologically diagnosed with melanoma were collected. The controls were those patients admitted to the same hospital for non-melanoma dermatological disease or non-melanoma skin cancer. All controls underwent a questionnaire and physical examination verifying that they had neither melanoma nor lesions clinically suggestive of melanoma. The cases and controls were age-matched by approximately five years. Two controls were assigned to each case

Sociodemographic variables, history of working outdoors and outdoor sports participation throughout life, insecticide exposure, smoking, sunburn history, and a family history of skin cancer were studied. Individual phenotypic features including skin phototype, eye color, hair color, and signs of sun damage were also studied.

Associations through the chi-squared test, Student's *t*-test and Wilcoxon rank-sum were used for statistical analyses and a multivariate analysis using conditional logistic regression was performed, with statistically significant,

clinically relevant, and potentially confounding variables included. Data were analyzed using the statistical software Stata.

This study included a total of 243 participants; 81 cases and 162 controls. The average subject age was 64 years. Analyzing the age by subtype, the patients with lentigo maligna averaged 67 years; the patients with acral lentiginous melanoma and nodular melanoma averaged 63 years; and those with superficial spreading melanoma averaged 58 years.

Of the total participants, 160 were women (66%) and 83 were men (34%). In the case group, the female percentage was 68% (55/81); in the control group, it was 65% (105/162). **Table 1** shows the histologic classification of the tumors. The most common melanoma subtype was acral lentiginous melanoma (32%), followed by lentigo maligna (29%). The melanomas were located mostly on the cheeks 21/81 (26%), nails 14/81 (26%), nose 11/81 (13%), and the soles of the feet 9/81 (11%).

Nearly 73% (59/81) of the cases had completed secondary school, compared with 71% (115/162) of the controls, which was not a significant difference ($p = 0.7$ by chi-squared test).

Table 2 shows the results of the bivariate analysis which reveals that having worked outdoors during early adult life (15–30 years old) increased the risk of developing melanoma by 1.9 times. The most frequent occupations among cases and controls in this period were farming activities (54% vs. 67%), construction (5% vs. 4%), and outdoor sales (11% vs.

Table 1 Histologic melanoma subtypes in the studied cases.

Histologic subtype	Cases ($n = 81$)	
	<i>n</i>	%
<i>In situ</i> melanomas		
Lentigo maligna	24	29.62
Other <i>in situ</i> melanomas	9	11.11
<i>Invasive</i> melanomas		
Acral lentiginous melanoma	26	32.09
Nodular melanoma	10	12.34
Superficial spreading melanoma	4	4.93
Lentigo maligna melanoma	4	4.93
Non-categorized malignant melanoma	4	4.93

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☆☆ Study conducted at the Centro Dermatológico Federico Lleras Acosta, Bogotá, Colombia.