

# Progressive macular hypomelanosis: an epidemiological study and therapeutic response to phototherapy

## Hipomelanose macular progressiva: estudo epidemiológico e resposta terapêutica à fototerapia

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**Abstract:** BACKGROUND: Progressive macular hypomelanosis is a common dermatosis in various continents. Its cause is unknown and proposed treatments have had little effect.

OBJECTIVES: To determine epidemiological aspects of progressive macular hypomelanosis in patients referred to a phototherapy clinic between 1997 and 2008 and to evaluate therapeutic response to PUVA (psoralen + UVA) photochemotherapy or narrowband UVB phototherapy.

METHODS: Eighty-four patients with progressive macular hypomelanosis were evaluated. After 16 phototherapy sessions, therapeutic response was classified as: unchanged, slightly improved (<50% of repigmentation), moderately improved (50-79% of repigmentation), much improved (80-99%) or cured (100%). After a minimum of three months, patients whose response was classified as cured or much improved were contacted by telephone to evaluate the persistence of the therapeutic response. RESULTS: Most of the patients were women (79%) and white (85%). Age at onset of progressive macular hypomelanosis ranged from 13 to 36 years. PUVA was prescribed for 27 patients and narrowband UVB phototherapy for 57. No significant difference was found between the outcomes obtained with PUVA and those obtained with narrowband UVB phototherapy (Fisher's exact test;  $p < 0.05$ ). The majority of patients (81%) had 50% or more repigmentation, with 65% being classified as cured or much improved. Nevertheless, there was a recurrence of the lesions in 72% of patients.

CONCLUSIONS: The fact that no patients were over 40 years of age suggests that progressive macular hypomelanosis is a self-limiting disease. Both PUVA and narrowband UVB are effective therapeutic options; however, they do not prevent recurrence of the disease.

Keywords: Phototherapy; Pigmentation disorders; Therapeutics

**Resumo:** FUNDAMENTOS: A hipomelanose macular progressiva é uma dermatose comum em diferentes continentes. Sua causa é desconhecida e os tratamentos propostos são pouco eficazes.

OBJETIVOS: Determinar aspectos epidemiológicos da hipomelanose macular progressiva em pacientes atendidos num setor de fototerapia, no período de 1997 a 2008, e avaliar a resposta terapêutica com PUVA ou UVBNB.

MÉTODOS: Foram avaliados 84 pacientes com Hipomelanose Macular Progressiva. Após 16 sessões de fototerapia, a resposta terapêutica foi definida: I=inalterado, MD=melhora discreta (< 50% de repigmentação), MM=melhora moderada(50-79%), MI=melhora intensa(80-99%) e C=cura(100%). Após um tempo mínimo de três meses, pacientes com cura ou MI foram contatados por telefone para avaliar a manutenção do resultado terapêutico.

RESULTADOS: Predominaram mulheres (79%) e a cor branca. A idade mínima de aparecimento da Hipomelanose Macular Progressiva foi de 13 anos e a máxima de 36 anos. Fototerapia com PUVA foi indicada em 27 pacientes e UVBNB em 57. Estatisticamente, não houve diferença significativa entre o tratamento com PUVA e UVBNB (teste de Fisher  $P > 0.05$ ). A maioria (81%) dos pacientes obteve 50% ou mais de repigmentação e 65% tiveram cura ou MI. Entretanto, 72% apresentaram recorrência das lesões.

CONCLUSÃO: A ausência de pacientes, com mais de 40 anos, sugere que a Hipomelanose Macular Progressiva seja uma doença autolimitada. Tanto PUVA como UVB NB são opções terapêuticas, porém não impedem a recidiva da doença.

Palavras-chave: Fototerapia; Terapêutica; Transtornos da pigmentação

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## INTRODUCTION

Progressive macular hypomelanosis (PMH) was described for the first time by Guillet et al. in 1980 as a pigmentation disorder of patients of mixed race (Black/Caucasian) resident in France and originating from the French Caribbean.<sup>1</sup> During the 1980s, the disease began to be reported in other countries; however, there was no association with mixed race and different nomenclatures such as progressive macular confluent hypomelanosis, *cutis trunci variata* and nummular and confluent hypomelanosis of the trunk were used to describe the condition.<sup>1,2</sup>

It is a common dermatosis in different continents such as Africa, Europe, Asia and the Americas. In Brazil, there are no epidemiological data on this dermatosis. Studies published in the literature describe a higher prevalence of the condition in females (7:1), and in adolescents and young adults with Fitzpatrick skin type II-IV.<sup>1,2</sup>

The condition is clinically classified by poorly defined, hypopigmented, confluent, nummular macules, located symmetrically in seborrheic areas, generally on the posterior and anterior trunk and, less commonly, on the neck and areas close to the extremities. The lesions are asymptomatic and there have been no precedents of inflammatory lesions.<sup>1-5</sup>

Its pathogenesis remains unclear. Some authors have suggested the effect of a subspecies of *Propionibacterium acnes* in the physiopathology of the condition.<sup>2,4</sup>

The treatment options that have been described in the literature include phototherapy (PUVA, UVA or narrow band UVB) and topical benzoyl peroxide 5% and clindamycin 1%. One report described treatment with oral doxycycline.<sup>1,6-8</sup>

The clinical course and prognosis of PMH have yet to be established. Some authors believe in the spontaneous disappearance of the lesions up to 10 years after the onset of the condition.<sup>6,9</sup>

The objectives of this study were to determine the epidemiological characteristics of PMH in patients attending a phototherapy clinic between 1997 and 2008 in the city of São Paulo, Brazil, and to evaluate the therapeutic response of this dermatosis to phototherapy (PUVA or narrow band UVB).

## MATERIAL AND METHODS

The medical charts of 84 patients with a clinical diagnosis of PMH, who had been treated with phototherapy (systemic PUVA or narrow band UVB) between 1997 and 2008 at a private phototherapy clinic, were evaluated retrospectively.

The epidemiological data referring to ethnicity, sex, age at the onset of the lesions and localization of the dermatoses were collected using standard ques-

tionnaires applied to all the patients prior to the initiation of phototherapy.

Up to 2002, patients were treated with PUVA (8-MOP at a dose of 0.4 mg/kg of weight) and from then onwards, when publications began to appear in the literature testifying to the treatment of various different pathologies with narrow band UVB, this wavelength of ultraviolet light began to be used. The initial dose of radiation was based on the phototype of each patient and then gradually increased in accordance with the patient's therapeutic response and the presence of side effects. The sessions occurred twice weekly and the therapeutic response was evaluated at the 16<sup>th</sup> treatment session. No other form of therapy was used in any of the cases.

The intensity of the therapeutic response was defined by the degree to which the lesions lightened in color: unchanged (no response), slightly improved ( $\leq 50\%$  of repigmentation), moderately improved (50-79% of repigmentation), much improved (80-99% of repigmentation) or completely cured (100% repigmentation). Data from the patients who abandoned treatment prior to the 16<sup>th</sup> session were excluded from the analysis of therapeutic response. After a minimum period of three months, the patients considered to have been completely cured or to have been much improved with therapy were contacted by telephone to evaluate whether the results obtained with phototherapy had persisted. Fisher's exact test was used to compare the response to treatment with PUVA and narrow band UVB.

## RESULTS

Of the 84 patients evaluated, 66 (79%) were female and 18 (21%) male. With respect to ethnicity, 71 (85%) were white and 13 (15%) non-white. Age at onset of the condition was  $20.83 \pm 5.01$  years (mean  $\pm$  standard deviation) (range 13 – 36 years).

With respect to the age of the patient at onset, 39 patients acquired the disease at 10-19 years of age, 40 at 20 to 29 years of age and only 5 patients reported onset at 30 years of age or older. The median time of progression of the disease prior to seeking medical attention was 3 years (interquartile range was 3) (range 1-19 years).

Twenty-seven patients were treated with PUVA, while 57 patients received narrow band UVB. Excluding those who failed to complete the 16 prescribed sessions, data were available for analysis from 20 patients who were submitted to PUVA and 37 patients submitted to narrow band UVB.

The therapeutic response of the 57 patients treated with phototherapy (PUVA or narrow band UVB) is shown in Table 1. Overall, for the two types of treatment, 22 patients (39%) were clinically cured,

**TABLE 1:** Progressive macular hypomelanosis: response to treatment with phototherapy

Response to treatment	PUVA phototherapy (n)	Narrow-band UVB phototherapy (n)	Total (n)/%
Cured	8	14	22 (39%)
Much improved	3	12	15 (26%)
Moderately improved	5	4	9 (16%)
Slightly improved	2	6	8 (14%)
Unchanged	2	1	3 (5%)
<b>Total</b>	<b>20</b>	<b>37</b>	<b>57 (100%)</b>

Degree to which the lesions lightened in color:  
 Cure: 100% repigmentation  
 Much improved: 80-99% repigmentation  
 Moderately improved: 50-79% repigmentation  
 Slightly improved: Up to 50% repigmentation  
 Unchanged: No response

15 (26%) were much improved, 9 (16%) were moderately improved and 8 (14%) improved slightly, while in 3 cases (5%), the patients' clinical condition remained unchanged. Clinical improvement of more than 50% was found in 46 patients (81%) and an improvement of over 80% in 37 patients (65%).

In table 2, patients have been grouped according to whether their response to treatment was 50% or better, or poorer than 50% and in accordance with the type of treatment to which they were submitted. Statistical analysis to compare these two groups, relating therapeutic response and the type of treatment (PUVA or narrow band UVB), showed no statistically significant difference (Fisher's exact test;  $p > 0.05$ ).

Telephone contact was established with 25 of the 37 patients who had been clinically cured or much improved: 14 of the 22 patients who had been cured and 11 of the 16 patients who had greatly improved. In the group of patients who had been cured, only 4 reported that the lesions were not present, while the other 10 reported a recurrence of the clinical condition. Of those who had improved greatly, 3 patients reported disappearance of the lesions, while 8 had PMH lesions. Overall, 7 (28%) of the patients who were contacted remained cured of their lesions (Table 3). Due to the small number of patients contacted, it was impossible to establish any correlation between outcome and the type of treatment given.

**DISCUSSION**

The prevalence of PMH remains unknown, although it appears to be a common disease in Brazil;

however, few epidemiological data are available in the Brazilian literature.

There was a predominance of female patients in the present sample (79% of the cases) and a greater frequency of the dermatosis in white individuals. The results on ethnic group and gender are in agreement with data published in the international literature. With respect to ethnicity, the sample studied here showed that PMH may occur in individuals of any color and that there was no effect of mixed race.

The youngest age at which the appearance of the dermatosis was reported was 13 years and the oldest 36 years. Only 5 patients (6%) were between 30 and 36 years of age at the time of onset of the symptoms. As already described, PMH was more common in adolescents and young adults in this sample. The absence of patients over 40 years of age suggests that PMH may be a self-limiting disease, as has already been reported in other studies.<sup>1,3,6</sup>

The time of progression of the disease was also found to be variable, ranging from 1 to 19 years.

In relation to treatment, phototherapy was found to be a good therapeutic option for this dermatosis, with over 80% of the patients achieving clinical improvement above 50% at the 16<sup>th</sup> session (Table 1). In 39%, the lesions were completely cured and in 26% the improvement in the patient's clinical condition was between 80 and 99%. It should be emphasized that many of the patients in the sample who improved greatly with the treatment continued beyond the initially prescribed 16 sessions and went on to achieve complete cure, which was confirmed

**TABLE 2:** Progressive macular hypomelanosis: comparison between response to treatment with PUVA and with narrow band UVB phototherapy

Response to treatment	PUVA phototherapy (n)	Narrow-band UVB phototherapy (n)	Total (n)
≥ 50% control	16	30	46
< 50% control	4	7	11
<b>Total</b>	<b>20</b>	<b>37</b>	<b>57</b>

Fisher's exact test:  $p = 0.5910$ .

**TABELA 3:** Hipomelanose macular progressiva: Evolução dos pacientes com controle do quadro clínico  $\geq$  80%, após mínimo de três meses do tratamento com fototerapia

Response to treatment	Cured (n)	Much improved (n)	Total N (%)
No lesions	4	3	7 (28%)
Lesions present	10	8	18 (72%)
<b>Total</b>	<b>14</b>	<b>11</b>	<b>25 (100%)</b>

Degree to which the lesions lightened in color:

Cured: 100% repigmentation

Much improved: 80-99% repigmentation.

following telephone contact in which three patients who had improved greatly at the 16<sup>th</sup> session then reported complete cure of their condition.

Comparing the clinical response between the groups treated with PUVA and narrow-band UVB and taking into consideration whether their clinical response was better or poorer than 50%, no statistically significant difference was found between the two groups (Table 2). Therefore, both PUVA and narrow-band UVB represent valid therapeutic options for PMH. In view of the ease of application of the treatment and the lower incidence of side effects, narrow-band UVB is suggested as the first line option. Nevertheless, of the patients contacted some time after treatment, the condition remained under control in only 28% of these cases (Table 3).

These data show that phototherapy is effective

for the control of PMH; however, results are temporary and there is a recurrence of the condition following the end of treatment.

### CONCLUSION

This study contributed with relevant epidemiological data, the first available in the Brazilian population, which is characteristically formed by individuals of mixed race. The data found were similar to those reported in the international literature, confirming the universal distribution of PMH, which appears not to be affected by climate or level of exposure to ultraviolet radiation.

Phototherapy was found to be effective for the control of PMH; however, it does not prevent recurrence of the disease. □

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