The use of lymecycline and benzoyl peroxide for the treatment of progressive macular hypomelanosis: a prospective study *

Uso da limeciclina associada com o peróxido de benzoíla no tratamento da hipomelanose macular progressiva: um estudo prospectivo

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Abstract: Progressive macular hypomelanosis is a dermatosis of uncertain etiology. The participation of Propionibacterium acnes has been suggested in view of the response achieved following therapy with drugs that are active against this bacterium. This report describes a series of thirteen patients with progressive macular hypomelanosis who were treated with an association of lymecycline and benzoyl peroxide over a three-month period. Response to treatment was excellent and the positive results were maintained during the entire follow up period.
Keywords: Pigmentation disorders; Benzoyl peroxide; Lymecycline.

Resumo: A hipomelanose macular progressiva é uma dermatose de etiopatogenia pouco conhecida. A participação do *Propionibacterium acnes* e a resposta ao tratamento com medicamentos com atividade para essa bactéria têm sido sugeridas. Relata-se uma série de casos de 13 pacientes com hipomelanose macular progressiva tratados com limeciclina e peróxido de benzoíla durante três meses, que apresentaram excelente resposta ao tratamento e nele se mantêm durante o período de seguimento do estudo.
Palavras-chave: Transtornos da pigmentação; Peróxido de benzoíla; Limeciclina

Progressive macular hypomelanosis (PMH) is characterized by hypopigmented, asymptomatic, non-scaly macules located on the trunk, which tend to be confluent in and around the midline, at times extending to the neck and upper segment of the limbs. [1-3] In some patients, transient repigmentation is seen following exposure to sunlight. [4]

The etiology of PMH is unknown and has been the subject of much research. [5] In a case series conducted in 2004 with 8 patients, Westerhof et al. detected *Propionibacterium acnes (P. acnes)* in all but one patient; the bacterium being isolated in anaerobic culture of biopsy specimens taken from follicular lesional skin. Additionally, the authors found follicular red fluorescence when examining the lesional skin of all the patients with a Wood's lamp. Since none of these findings were seen on healthy follicular skin, it was suggested that *P. acnes* may play a role in the etiopathogenesis of the dermatosis.

The hypothetical association between *P. acnes* and the etiopathogenesis of PMH has motivated some investigators to use medication that is active against this bacterium, opening new prospective avenues of therapy, since no treatment was available for this dermatosis up to that time. [2,6,7]

In 2006, Relyveld et al. conducted a comparative study of 45 patients with PMH using a lotion containing 5% benzoyl peroxide and 1% clindamycin on one side of the trunk and a cream with 0.05% fluticasone on the other side. After exposing the skin to ultraviolet A radiation, significant repigmentation was seen ($p<0.001$) on the side of the back on which the combination of benzoyl peroxide and clindamycin was applied, giving strength to the hypothesis that *P. acnes* plays a role in the etiopathogenesis of PMH. On the other hand, in 2010 Duarte et al. treated 84 patients using only phototherapy and reported repigmentation of 50% or more in 81% of these patients. Nevertheless, there was a recurrence of the lesions in 72% of these cases. [8]

The use of tetracycline derivatives for the treatment of acne is already widely known and these antibiotics have

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been considered the treatment of choice, not only because of their effect against *P. acnes* but also because of their potent antiinflammatory effect, leading to reduced neutrophil chemotaxis and inhibitory effects on cytokines. [9,10]

In 2008, Perman et al. reported repigmentation of PMH lesions following a 6-week course of treatment with doxycycline. Later, Almeida et al. (2009) reported similar results in 11 patients with PMH following the use of 100 mg of minocycline daily for three months, giving further strength to the hypothesis of a probable role of *P. acnes* in the development of this dermatosis.

Lymecycline is a second-generation tetracycline that has a better pharmacokinetic profile, can be administered in the form of a single daily dose and may be taken during meals. It also has fewer side effects. The oral antibiotics used to treat *P. acnes* should be administered in association with benzoyl peroxide to minimize bacterial resistance and increase the efficacy of the treatment. [9]

Based on the hypothesis of the participation of *P. acnes* in PMH, the objective of this report was to demonstrate the clinical efficacy of the use of 300 mg of lymecycline daily in association with 5% benzoyl peroxide at night for 12 weeks.

Thirteen patients with a diagnosis of PMH were included in this study. The patients were instructed to expose themselves to the sun three times a week for 30 minutes. They were evaluated clinically and also by comparing photographs at monthly intervals during treatment, then one month after treatment and every three months thereafter for a year.

One patient abandoned the study because he moved away. In accordance with clinical evaluation and the analysis of photographs, an improvement of 90% or more was found in 10/12 patients (83.3%) at the end of the treatment and during the follow-up period, as evaluated by the dermatologists involved in the study, in a consensus. In the opinion of the patients themselves, this improvement occurred in 11/12 patients (91.6%) (Figures 1 and 2).

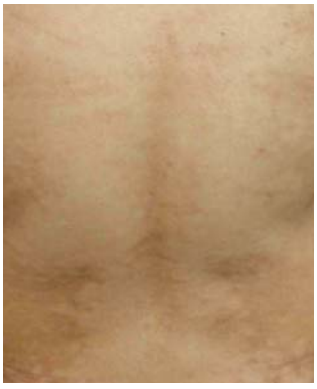

Figure 1: Prior to treatment: Multiple coalescent hypopigmented macules covering the patient's back

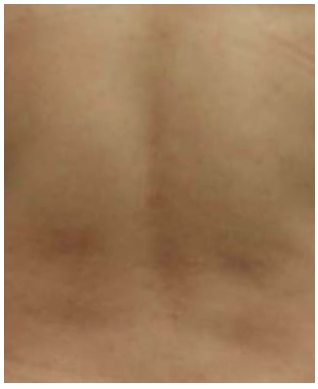

Figure 2: Following treatment: Disappearance of the macules 9 months after the end of treatment with lymecycline associated with benzoyl peroxide

Persistent therapeutic success was achieved in one patient six months after the end of treatment, in four patients at nine months and in two patients at one year. One patient had a recurrence of a few lesions seven months after the end of treatment. With respect to the other patients, their lesions had regressed by the end of the treatment but they failed to return for follow-up evaluation.

The excellent response to treatment, which remained during the entire follow-up period of the study, shows this to be a novel treatment option for this dermatosis, which, despite being asymptomatic, has psychosocial repercussions, affecting patients' self-esteem. Nevertheless, controlled, blinded and prospective studies should be performed with larger sample sizes to evaluate the actual effect of the use of these drugs in the treatment of PMH and to determine the possibility of relapses over the long term. ❑

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