Benzoyl peroxide/clindamycin/UVA is more effective than fluticasone/UVA in progressive macular hypomelanosis: A randomized study

Germaine N. Relyveld, MD,[a] Melanie M. Kingswijk,[a] Johannes B. Reitsma, MD, PhD,[b] Henk E. Menke, MD, PhD,[c] Jan D. Bos, MD, PhD,[d] and Wiete Westerhof, MD, PhD[a]
Amsterdam and Rotterdam, The Netherlands

Background: There is no effective treatment for progressive macular hypomelanosis. Recent findings indicate that *Propionibacterium acnes* may play a role in the pathogenesis.

Objectives: We sought to compare the effectiveness of antimicrobial therapy with anti-inflammatory therapy in patients with progressive macular hypomelanosis.

Methods: A total of 45 patients were randomized to a within-patient left-right comparison study of benzoyl peroxide 5% hydrogel/clindamycin 1% lotion in combination with UVA irradiation versus fluticasone 0.05% cream in combination with UVA irradiation. Repigmentation was determined by photometric measurements of changes in skin color and by patient and dermatologist assessment using before and after photographs.

Results: Benzoyl peroxide 5% hydrogel, clindamycin 1% lotion, and UVA led to better repigmentation than fluticasone 0.05% cream in combination with UVA irradiation in all measurements. (Photometric measurements $P = .007$, patient assessment $P < .0001$, and dermatologist assessment $P < .0001$.)

Limitations: There was difficult objective color measurement. Therefore, subjective assessment has important additional value. Right-left comparisons have certain inherent limitations.

Conclusion: Antimicrobial therapy in conjunction with light was more effective in repigmentation in patients with progressive macular hypomelanosis than a combination of anti-inflammatory therapy and light. (J Am Acad Dermatol 2006;55:836-43.)

Progressive macular hypomelanosis (PMH) is a skin disorder of the trunk, rarely extending to the neck/head region, proximal extremities, or both, characterized by ill-defined, nummular, symmetrically localized hypopigmented macules. In the majority of patients, a hypopigmented area is present on the front and the back of the trunk that seems to originate from confluence of the macules.[1-5] Diagnostic criteria include characteristic clinical features as described above and the presence of red follicular fluorescence in hypopigmented spots that is absent in adjacent normal skin. Pityriasis versicolor is excluded by negative potassium hydroxide test results of epidermal scrapings. PMH might be more common in tropical and subtropical countries, but prevalence studies are scarce. In 1994, Lesueur et al[3] diagnosed 121 cases of PMH during a screening for leprosy among 511 patients in the French West Indies

Abbreviations used:

bcUVA:	benzoyl peroxide 5% hydrogel, clindamycin 1% lotion, and UVA
CIE:	Commission International de l'Éclairage
fUVA:	fluticasone and UVA
PMH:	progressive macular hypomelanosis

From the Netherlands Institute for Pigment Disorders,[a] Department of Clinical Epidemiology and Biostatistics,[b] and Department of Dermatology,[d] Academic Medical Center, University of Amsterdam; and Department of Dermatology, Sint Franciscus Gasthuis, Rotterdam.[c]
Funding sources: None.
Conflicts of interest: None identified.
Reprint requests: W. Westerhof, MD, PhD, Netherlands Institute for Pigment Disorders, Meibergdreef 35, 1105 AZ Amsterdam, The Netherlands. E-mail: W.Westerhof@amc.uva.nl.
0190-9622/$32.00

doi:10.1016/j.jaad.2006.03.020

(Martinique). Guillet et al[2] diagnosed 150 new cases per year in their dermatology clinic in Martinique. Little is known about the origin and pathogenesis of PMH. Ultrastructural studies conducted by Guillet et al in 1988[1] showed stage IV single melanosomes in nonlesional skin and small type stage I to III aggregated melanosomes in lesional skin of patients from mixed (Negroid-Caucasoid) background.

In 2004, Westerhof et al[6] proposed that PMH is caused by *Propionibacterium acnes*. This suggestion was based on the observation that illumination of the hypopigmented spots with a Wood's lamp in a dark room produces a red follicular fluorescence, which is absent in normal adjacent skin. This was further substantiated by culturing *P acnes* from pilosebaceous ducts of lesional skin. The hypothesis was formulated that *P acnes* produces a factor that interferes with melanogenesis, leading to hypopigmented macules. Eliminating *P acnes* with topical antibacterial therapy, such as in acne, could, therefore, improve repigmentation in patients with PMH. A combination therapy of clindamycin lotion and benzoyl peroxide hydrogel would be recommended because research has shown that in patients with mild to moderate acne this combination has significantly better results than either of the two components alone. Furthermore, benzoyl peroxide combined with topical antibiotics reduces the risk that resistant strains of *P acnes* develop.[7-9] Another view on the pathogenesis, based on our histologic examination showing mild perifollicular lymphocytic infiltration,[6] is that hypopigmentation is secondary to an inflammatory process, although there are no clinical signs of inflammation in PMH. This would suggest that anti-inflammatory agents such as topical corticosteroids could be a possible treatment.

We conducted a trial to examine whether antibacterial treatment is more effective in repigmentation than anti-inflammatory treatment in patients with PMH.

METHODS

We performed a within-patient, left-right randomized trial comparing benzoyl peroxide/clindamycin in combination with UVA (bcUVA) with fluticasone in combination with UVA (fUVA) in patients with PMH. The medical ethical committee of the hospital approved the study protocol and written consent was obtained from all patients.

Patients

Patients with PMH between 16 and 55 years of age were eligible for inclusion. The diagnosis of PMH was based on clinical findings including the presence of red follicular fluorescence in the hypopigmented spots when illuminated with a Wood's lamp in a dark room. Patients were excluded if they: had positive potassium hydroxide test results; were sensitive to any of the study medication ingredients or sunlight; were treated with chemical peeling or other treatments that could cause scaling of the trunk; or were pregnant or lactating. In addition, any previous treatment for PMH or any antibacterial treatment (both local and systemic) had to be stopped at least 3 months before study entry.

Interventions

Patients received instructions for daily application of benzoyl peroxide 5% hydrogel at night and clindamycin 1% lotion in the morning on one side (antibacterial treatment) and fluticasone cream 0.05% at night on the other side (anti-inflammatory treatment). A computerized randomization program was used by the treating physician to decide which side received which therapy. Patients and the treating physician were not blinded for treatment allocation.

Patients applied the medication themselves during a period of 14 weeks. During this period, patients exposed both sides to UVA light for 20 minutes 3 times a week. For this purpose they received a half-body solarium (HB 406, Philips, Eindhoven, the Netherlands) and were instructed to sit at a distance of 55 cm in front of the solarium. After 20 minutes at this distance, the effective flux on the skin (H-IECeff) is 233 J/m^2.

All treatments were stopped after 14 weeks, but patients were instructed to stay out of the sun for an additional period of 12 weeks. If sun exposure could not be avoided, patients were advised to apply a sunscreen with a protecting factor of at least 30 every 2 hours.

Objective skin color measurements

The primary outcome in our trial was the difference in repigmentation between bcUVA- and fUVA-treated areas as measured by the colorimeter. We measured skin color at baseline; after 2, 6, 10, and 14 weeks of treatment; and after a period of 12 weeks without treatment (t = 26 weeks), using a spectrocolorimeter (Microflash 200d, Datacolor, Lawrenceville, NJ). This colorimeter uses a system devised in 1976 by the Commission International de l'Éclairage (CIE). Various investigators have extensively used the technique to quantitatively compare erythema, pigmentation, and skin color.[10-12] It transforms a reflectance spectrum R (λ) into 3 values: L*, a*, and b*. L* represents the lightness of the spectrum and varies from 0 for a black object to 100 for a white object, a* represents green (negative values) and red (positive values), and b* represents blue (negative values) and