Depigmentation Therapies for Vitiligo

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KEYWORDS

• Depigmentation • Vitiligo • Pigmentary disorders • Disorders of appearance
• Monobenzyl ether of hydroquinone • MBEH • 4-Methoxyphenol • Mequinol

KEY POINTS

- The general goals of medical management of vitiligo are to repigment affected areas of skin and to stabilize the progression of depigmentation.
- However, for some patients with vitiligo affecting extensive body surface areas who are unresponsive to repigmentation therapies, depigmentation of the remaining normal skin may be a better choice.
- Candidates for depigmentation therapy should be carefully screened and patient education is essential.
- Permanent topical therapies used for depigmentation include monobenzyl ether of hydroquinone, 4-methoxyphenol, and 88% phenol. Physical modalities, such as cryotherapy and lasers, are also being used successfully.

INTRODUCTION

Vitiligo is a common acquired disorder of the epidermis and hair follicles that manifests clinically as progressive depigmentation due to loss of functioning melanocytes. It affects 1% to 2% of the global population.[1] Studies suggest an equal incidence in all racial-ethnic groups. However, because of the highly visible contrast between the constitutive skin color and the white patches, vitiligo can be particularly disfiguring in darker-complexioned skin types.[2,3] Given the disfiguring aspect of the disease, vitiligo can profoundly impact the quality of life in children and adults.[4,5]

Multiple theories have been proffered for the pathogenesis of vitiligo, including autoimmune, biochemical, oxidative stress, neural, melanocytorrhagy and viral mechanisms.[2] However, multiple recent studies document the expanding role of immune mechanisms in the pathogenesis of vitiligo.[6,7]

In general, therapies for vitiligo address stabilization of the disease and repigmentation of affected sites. Stabilization agents include systemic corticosteroids, oral mini-pulse corticosteroid therapy, minocycline, and methotrexate. First-line therapies for repigmentation are calcineurin inhibitors, topical corticosteroids, and narrow band (NB)-UVB phototherapy. Although many patients achieve successful repigmentation outcomes, others develop progressive disease affecting extensive body surface areas and fail to respond to repigmentation protocols. The goal for such patients with extensive disease would be to create a uniform skin tone by depigmenting the remaining pigmented skin sites.

CANDIDATES FOR DEPIGMENTATION THERAPY

Depigmentation therapy can be a viable therapeutic alternative in patients with extensive disease

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affecting greater than 30% to 40% of body surface areas.[2,3,8]

Most patients who choose depigmentation have failed to achieve optimal repigmentation. Depigmentation therapy can be used in all skin types devastated by the contrasting areas of normal and vitiliginous skin. Patient selection is of paramount importance, given the permanency of depigmentation therapy (**Box 1**). Prospective patients should be carefully screened. A detailed medical history should be obtained including any history of psychiatric illness portending unrealistic therapeutic outcomes.[9] An extended consultation should be conducted with patients and their families when possible. Issues that should be discussed in depth are included in **Box 2**. It is imperative that potential patients thoroughly understand the permanent nature of the process. It is important with younger patients and their families to explain that if medical advances provide new therapies for repigmentation, they may not be candidates for such therapies if they have undergone depigmentation.[10] All patients treated at the Vitiligo & Pigmentation Institute of Southern California sign an informed consent before initiating depigmentation therapy. A sample template of the authors' informed consent is included in **Box 3**.

The decision to undergo depigmentation of areas of normal skin is especially complex. For example, the decision may be more complicated for African Americans and Asians by the continued presence of secondary racial characteristics, such as facial features and hair texture. Thus, the potential sociocultural issues should be thoroughly explored with patients before initiating therapy.

TOPICAL DEPIGMENTATION THERAPIES

The most readily available depigmenting agents include monobenzyl ether of hydroquinone (MBEH), 4-methoxyphenol (4MP, mequinol or p-hydroxyanisole) and phenol (**Table 1**). In addition, physical therapies, such as lasers and cryotherapy, both as monotherapy and as adjuncts to topical treatments, are also used for depigmentation.

Depigmentation is a gradual process characterized by gradual progressive fading of patients' unaffected normal pigmentation. Complete depigmentation may require 1 to 3 years of treatment. In the authors' experience, most patients are satisfied with the therapeutic outcomes.

Box 1
General indications and inclusion criteria for depigmentation therapy

- Patients with severe disease affecting greater than 30% or 40% body surface areas who have failed repigmentation therapies
- Patients with severe disease affecting greater than 30% or 40% depigmentation who are unable to undergo the time and rigors of repigmentation therapies
- Emotionally stable patients
- Patients willing to adhere to photoprotection
- A willingness to accept the inability to tan

Box 2
Issues for discussion with prospective patients

- Permanency of the treatment
- Realistic expectations
- Color match with areas of depigmentation
- Treatment time and cost
- Mechanism of action of the drug, including depigmentation at sites distal to areas of use
- Drug-related side effects
- The potential for patchy repigmentation
- Consort depigmentation with inappropriate use

Monobenzyl Ether of Hydroquinone

MBEH (p-benzyloxy-phenol, monobenzone) is the only topical depigmenting agent that is currently approved for vitiligo by the Food and Drug Administration. Moreover, the only indication for use of the drug is in patients with vitiligo (**Figs. 1** and **2**). It is a hydroquinone (HQ) derivative. MBEH was ushered into the realm of dermatology in the late 1930s following seminal observations by McNally[11] and Oliver and colleagues.[12,13] They reported that workers exposed to MBEH, which was used as an antioxidant in the rubber tannery industry, developed depigmentation. Tannery workers developed white patches at the site of chemical contact from their rubber gloves that contained Agerite Alba (MBEH). Depigmentation also developed at sites distal to exposure to the chemical.

Although MBEH is structurally related to HQ, commonly used as a hypopigmenting agent, it has not been associated with the development of exogenous ochronosis. This condition is a rare but serious complication of prolonged use of HQ frequently seen in users of over-the-counter skin bleaching creams. MBEH remains the first-line agent for depigmentation in patients with vitiligo.