Current and emerging treatments for vitiligo

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Learning objectives
After completing this learning activity, participants should be able to choose an optimal approach to management of all patients with vitiligo; list the risks associated with treatment for vitiligo; and discuss emerging treatment options for vitiligo.

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The editors involved with this CME activity and all content validation/peer reviewers of the journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

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Clinicians should be aware that vitiligo is not merely a cosmetic disease and that there are safe and effective treatments available for vitiligo. It is important to recognize common and uncommon presentations and those with active disease, as well as their implications for clinical management; these were discussed in the first article in this continuing medical education series. Existing treatments include topical and systemic immunosuppressants, phototherapy, and surgical techniques, which together may serve to halt disease progression, stabilize depigmented lesions, and encourage repigmentation. We discuss how to optimize the currently available treatments and highlight emerging treatments that may improve treatment efficacy in the future. (J Am Acad Dermatol 2017;77:17-29.)

Key words: afamelanotide; biologics; corticosteroids; excimer lamp; excimer laser; grafting; leukoderma; methotrexate; narrowband ultraviolet light; phototherapy; pigmentation; tacrolimus; treatment; vitiligo.

MEDICAL TREATMENTS

Key points

- **Potent or ultrapotent topical corticosteroids administered in a cyclical fashion avoids adverse effects**
- **Topical tacrolimus 0.1% should be used twice daily for affected areas on the face and intertriginous areas**
- **Narrowband ultraviolet B light phototherapy appears to be safe and effective when >5-10%**

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body surface area is affected; focused narrowband ultraviolet B light phototherapy, such as hand and foot units or excimer laser, is useful in localized disease

- **Topical tacrolimus 0.1% used twice per week may help prevent relapse after repigmentation is achieved**

Vitiligo is not a "cosmetic disease,"[1] so treatment can and should be offered to patients. The optimal treatment of vitiligo will first depend on the subtype of the disease, percent of body surface area (BSA) involved, effect on quality of life, and the perception of the patient concerning the risk to benefit ratio. For example, in the segmental variant of vitiligo, the disease follows a predictable course, with a phase of rapid spreading and early hair follicle involvement restricted to the affected segment lasting 3 to 24 months. This is usually followed by complete stabilization. The segmental variant is therefore more difficult to treat and requires early medical intervention or a surgical approach late in the disease course. With all types of vitiligo, timing of treatment is an important predictor of success, with early disease responding best.[2]

In contrast to the segmental variant, most cases of vitiligo follow an unpredictable course, with periods of disease progression and quiescence. Early involvement of the hair follicle is uncommon.[3] Spontaneous repigmentation has been described, although this is not the rule. At present, no medical treatment for repigmenting vitiligo has been approved by the US Food and Drug Administration (FDA), and therefore treatments are used off-label. Topical treatments may be applied alone when small areas are involved or when other treatment modalities are not readily available. Phototherapy combined with topical treatment is preferred when >5-10% of the BSA is affected or when focal areas are unresponsive to topical treatments alone.

Topical corticosteroids (level II evidence)

When selecting a topical steroid, the site of the lesion and age of the patient should be considered. Lesions on the body may be treated with ultrapotent or potent corticosteroids; the face, neck, and intertriginous areas and lesions in children should be treated with either midpotency topical corticosteroids or calcineurin inhibitors (see below). Possible regimens include daily or twice daily application in a cyclical fashion with "days off" (eg, 1 week on then 1 week off for 6 months, or application for 5 consecutive days followed by 2 days off).[4] In practice, these regimens appear to minimize the risk of adverse effects, although evidence-based studies to support this are lacking.

Topical calcineurin inhibitors (level II evidence)

In recently published guidelines, the European Dermatology Forum group proposed twice daily topical calcineurin inhibitors for head and neck lesions as a first-line approach.[5] This recommendation is based on a combination of its efficacy in these sites and its favorable side effect profile.[6,7] Warnings have been placed on the long-term use of tacrolimus because of a theoretical long-term risk of cancer, despite its repeatedly demonstrated safety.[8] Other than exposure to medically administered phototherapy or excimer laser, photoprotection should be encouraged when using topical immunosuppression. When using a cyclical regimen for topical steroids outlined above, calcineurin inhibitors may be used on the "off" days to provide consistent treatment without increasing the risk of adverse events.

Phototherapy

There are 2 main indications for the use of whole-body phototherapy in vitiligo: extensive disease (>5-10% of BSA) and rapidly spreading disease. However, patients with smaller areas of involvement and less activity may also require phototherapy in some instances because of its superior efficacy. With all medical interventions, the physical and psychological impact of the disease should be weighed against the risks of a particular treatment, which typically requires physicians to customize the management strategy for each patient. In general, patients should not apply any topical medications or sunscreen before ultraviolet (UV) light therapy in order to avoid reduced transmission of UV light into the skin. Patients should also be vigilant about sun protection to avoid additive effects of sun exposure when receiving UV light therapy treatment.

Psoralen plus ultraviolet A light phototherapy (level I evidence)

Psoralen plus ultraviolet A light phototherapy (PUVA) was the first phototherapy regimen used in patients with vitiligo. The results were reasonable, but issues with compliance (eg, oculocutaneous protection), side effects (eg, nausea), and an increased risk of skin cancer led to a decline in its use. In a recent Cochrane review, PUVA was deemed inferior to narrowband ultraviolet B light therapy (NB-UVB) in achieving >75% repigmentation in the general population of vitiligo patients.[6] Therefore, PUVA has been largely replaced by NB-UVB, although PUVA may still induce faster repigmentation.[9,10] PUVA may be considered in patients with